

Detecting incipient inner-ear damage from impulse noise with otoacoustic emissions

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Audiometric thresholds and otoacoustic emissions (OAEs) were measured in 285 U.S. Marine Corps recruits before and three weeks after exposure to impulse-noise sources from weapons' fire and simulated artillery, and in 32 non-noise-exposed controls. At pre-test, audiometric thresholds for all ears were ≤ 25 dB HL from 0.5 to 3 kHz and ≤ 30 dB HL at 4 kHz. Ears with low-level or absent OAEs at pre-test were more likely to be classified with significant threshold shifts (STSs) at post-test. A subgroup of 60 noise-exposed volunteers with complete data sets for both ears showed significant decreases in OAE amplitude but no change in audiometric thresholds. STSs and significant emission shifts (SESSs) between 2 and 4 kHz in individual ears were identified using criteria based on the standard error of measurement from the control group. There was essentially no association between the occurrence of STS and SES. There were more SESs than STSs, and the group of SES ears had more STS ears than the group of no-SES ears. The increased sensitivity of OAEs in comparison to audiometric thresholds was shown in all analyses, and low-level OAEs indicate an increased risk of future hearing loss by as much as ninefold.

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I. INTRODUCTION

Otoacoustic emissions (OAEs) are more sensitive than pure-tone audiometric thresholds in detecting the early stages of permanent noise-induced inner-ear damage in humans. Typical results for noise-exposed *groups* followed longitudinally show a decrease in OAE amplitudes, but no change in audiometric thresholds (Engdahl *et al.*, 1996; Murray *et al.*, 1998; Murray and LePage, 2002; Konopka *et al.*, 2005; Seixas *et al.*, 2005a, 2005b; Lapsley Miller *et al.*, 2006).¹ Most longitudinal studies do not last long enough to also see hearing loss in the noise-exposed group. A recent finding is that low-level or absent OAEs in noise-exposed *individual* ears may be a risk factor or predictor for hearing loss in their near future for continuous noise overlaid with impact noise (Lapsley Miller *et al.*, 2006). It is of interest to know for both

theoretical and clinical reasons whether this finding generalizes to impulse noise.

Impulse noise is a common occupational and recreational hazard (Clark, 1991; Humes *et al.*, 2005). The waveform of the impulse as received at the ear is shaped by the individual pinna, ear canal, and middle ear, which may have an activated middle-ear reflex, sometimes even prior to the noise exposure in the case of an anticipatory reflex (e.g., Marshall *et al.*, 1975). To add to the complexity, higher-level sounds may result in less stapes motion and thus less damage than lower-level sounds (e.g., Price, 2007). In a work setting with considerable impulse-noise exposure (both self-generated and from other sources in the environment), as is the case for some military jobs, the impulse-noise exposure for any one individual can be difficult to quantify (unless one has the luxury of a microphone in the ear canal). We expect more variability in the noise exposure to the cochlea across these individuals than for individuals working in steady-state background noise, such as an engine room, where the noise exposure is more homogenous.

If the noise exposure reaching the cochlea is more variable across individuals and if a single exposure can cause inner-ear damage, we expect that the state of the inner ear

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prior to the noise exposure will not be as predictive of incipient risk for this group of people as for a group of people with more uniform noise exposure.

Noise exposure from live-fire training can produce hearing loss very quickly. Permanent threshold shifts (PTSs) have been reported in 10% or more of military personnel during weapons' training, including 300 rounds of M-16 live-fire training,² Army special forces undergoing routine weapons' training,³ and Israeli army recruits firing an average of 420 M-16 rounds (Attias *et al.*, 1994), all in spite of wearing hearing protection. In the current study, Marine recruits undergoing basic training were chosen because some PTS within a short amount of time was expected, and the overall amount of noise exposure for each volunteer would be very similar.

The current study is complementary to the study reported in Lapsley Miller *et al.* (2006). The same experimental protocol was used, with each volunteer receiving both pure-tone audiometry and OAE tests before and after a significant multiday noise exposure in a military operational setting. The primary difference between the two studies is the type of noise exposure—with impulse-noise exposure (from weapons' fire) in the current study, in contrast to continuous noise overlaid with impact noise (from aircraft and machinery noise) in the previous study. The current study is also a subset of a larger interdisciplinary study investigating the auditory and genetic determinants of susceptibility to noise-induced hearing loss (NIHL).

II. METHOD

A. Participants

The study participants were 401 male volunteers who had just begun mandatory basic training as U.S. Marine Corps recruits.⁴ No female volunteers were available, as this military installation provided training to male recruits only. Two experimental groups were formed from the volunteers who met the screening criteria and completed the study: the noise-exposed group ($N=285$; age at enrollment: range 17.4–28.1 years, median=19.2 years); and the control group (who were not exposed to noise between pre- and post-tests; $N=32$; age at enrollment: range 18.2–27.1 years, median =20.0 years).

Each group was tested twice with an identical protocol. Test times were determined by the recruit training schedule. The pre-test measurements occurred one to six weeks prior to the noise exposures (all volunteers had been noise-free for at least a day), and the post-test measurements occurred three weeks after the noise exposures. At pre-test, volunteers were screened for clear ear canals, audiometric thresholds of ≤ 25 dB HL from 0.5 to 3 kHz and ≤ 30 dB HL at 4 kHz, and peak immittance within the range of ± 50 daPa atmospheric pressure, with grossly normal amplitude, slope, and smoothness of the tympanogram. Volunteers who met these screening criteria proceeded to OAE testing. Volunteers who did not meet the screening criteria did not enroll in the study. At post-test, volunteers were checked for clear ear canals (cerumen was removed if present) and peak immittance

within the range of ± 50 daPa atmospheric pressure, with grossly normal amplitude, slope, and smoothness of the tympanogram.

Between test sessions, the noise-exposed group received impulse-noise exposures (M-16 rifle, M-60 machine gun, and C-4 explosives) as prescribed by standard operating procedures.⁵ A 5%–10% incidence of permanent hearing loss was expected, despite mandatory hearing protection. The volunteers in the control group were recruits who were in a “medical hold” status for minor nonauditory injuries, and a few U.S. Navy medical personnel. They were tested on two occasions within a 24–48 h period without any weapons' noise exposures before or between tests.

Data collection occurred from January to September 2000.

B. Noise exposures

During basic training, the noise-exposed group underwent approximately three and a half weeks of training that involved weapons' noise exposures at Marine Corps Base, Camp Pendleton, CA. All recruits spent six days on outdoor rifle ranges, where each individual fired 340 rounds with an M-16 rifle (~ 157 dB pSPL, US Army Center for Health Promotion and Preventive Medicine, 2008). Next, they made three 20–30 min runs through a combat obstacle course where they were exposed to M-60 machine-gun fire (~ 155 dB pSPL, US Army Center for Health Promotion and Preventive Medicine, 2008) and simulated artillery using C-4 explosives. Noise measurements performed with the Quest M-27 noise logging dosimeter revealed both the simulated artillery and C-4 explosions produced levels in excess of 146 dB pSPL (maximum limits of the M-27). Noise sources were located 5–20 ft from volunteers' ears depending on where individuals were located on the course at the time of an impulse-noise presentation. Finally, there were several days of simulated-combat exercises where each recruit fired an additional 50–75 M-16 rounds, as well as exposure to more M-60 machine-gun fire and simulated artillery using C-4 explosives. Because other recruits were simultaneously firing M-16 rounds on the rifle range and during combat exercises, each individual was exposed to more than the 390–415 rounds they fired from their own weapons. The exact number of M-16 rifle-fire exposures for each volunteer was not measured. The recruits fired from three positions: lying down in a prone position, in a sitting position, and standing up. The majority of the rounds fired were in the prone position (80%). The noise exposures were very similar for each volunteer for the rifle range and obstacle course, but there was a lot more variability in exposures through the simulated-combat exercises. The rest of the time, the recruits' activities were severely restricted, and they were not exposed to any significant levels of nonmilitary noise.

The recruits were provided with foam, disposable E·A·R Classic (Aearo Corporation) earplugs each day on the rifle range, obstacle course, and during combat exercises. These earplugs come in one size only and have a noise reduction rating of 29 dB (Berger, 2000), but only if properly and deeply fitted. The drill instructors informed large groups

of recruits how to use the earplugs. Because individual fitting was not done and only one size was provided, the actual field attenuation no doubt was much less than optimal.

C. Audiometric equipment, stimuli, and testing

Audiometric testing was performed using either a Maico MA-1000 PC audiometer or a Grason-Stadler G-117 portable audiometer. Pure-tone stimuli were delivered through Telephonics TDH-49 supra-aural earphones in MX41/AR cushions. Audiometers were calibrated (ANSI, 1996), and daily calibration and listening checks were performed each day of testing (Navy Occupational Health and Safety Program, 1999). Audiometric testing was performed one volunteer at a time in double-walled sound-attenuating chambers (ANSI, 1991). Earphone placement was checked by the examiner. At the pre-test audiogram, the recruits had been without much sleep for one to two nights. This necessitated the examiner being in the same room as the volunteer, testing him similarly to a pediatric patient (e.g., frequent animated verbal interaction and encouragement) to maintain alertness.

Audiometric thresholds were measured in both ears (the left ear was always tested first), using the standard U.S. Navy hearing-conservation program test protocol, which is an ascending, modified Hughson–Westlake procedure, with a 5 dB step size and frequencies tested in the order of 1, 0.5, 1, 2, 3, 4, and 6 kHz (Navy Occupational Health and Safety Program, 1999). All audiograms were collected manually by qualified technicians or audiologists.

Note that we did not use the results of the group hearing testing typically done for marine recruits as they enter basic training, because it was not reliable enough for our purposes (automated audiometry with up to eight recruits at a time in the booth).

D. Tympanometry equipment, stimuli, and testing

Middle-ear pressures were estimated from the peak of an immittance tympanogram with a 226 Hz tone using a Grason-Stadler GSI 33 version 2 analyzer at a sweep speed of 12.5 daPa/s to minimize hysteresis.

E. Otoacoustic emission equipment, stimuli, and testing

Two types of OAEs were measured: transient-evoked otoacoustic emissions (TEOAEs) and distortion-product otoacoustic emissions (DPOAEs). Both OAE types were measured with the ILO292 Echoport system (Otodynamics Ltd., England), using the DPOAE probe. To allow better placement and manipulation in the ear canal, an acoustic-immittance probe tip (which had been enlarged using a grinding tool) was inserted onto the DPOAE probe. The size of the probe tip was matched to the size of the ear canal, and was noted so that the same size could be used for the pre- and post-tests. Individual in-the-ear calibration was used for both TEOAE and DPOAE measurements. OAE testing was performed two volunteers at a time, with two testers also present, in a double-walled sound-attenuating chamber (ANSI, 1991).

An identical test battery was used as for Lapsley Miller *et al.* (2006). Before OAE testing (for both pre- and post-tests), an otoscopic examination was conducted with cerumen removal if necessary, and peak immittance was measured to ensure it was within ± 50 daPa atmospheric pressure in both ears.

TEOAEs were evoked with a 74 dB pSPL click, presented in nonlinear mode, where responses to three clicks at one polarity and one click with opposite polarity and 9.5 dB higher were added together to reduce linear artifact from the stimulus (Bray, 1989). At pre-test, every attempt was made to get a flat stimulus spectrum during calibration by manipulating the depth and angle of the probe tip in the ear canal. At post-test, every attempt was made to get the same stimulus pattern during calibration as in the pre-test by referring to a screenshot printed out after the first test. TEOAEs were collected and averaged until 260 low-noise averages were obtained. The results were windowed (2.5 ms onset delay, 20.5 ms duration, with 2.56 ms rise/fall) and filtered (0.683–6.103 kHz bandpass filter), then analyzed into half-octave bands (0.7, 1, 1.4, 2, 2.8, 4, and 5.6 kHz).

In order of presentation, DPOAEs were measured with stimulus levels $L_1/L_2=57/45$, $59/50$, $61/55$, and $65/45$ dB SPL (abbreviated herein to $DP_{57/45}$, $DP_{59/50}$, $DP_{61/55}$, and $DP_{65/45}$). For all stimulus levels, the f_2/f_1 ratio was 1.22, with $f_2=1.8, 2.0, 2.2, 2.5, 2.8, 3.2, 3.6, 4.0,$ and 4.5 kHz.

F. Data definitions, cleaning, and reduction

The short testing time available for each volunteer meant that it was not always possible to obtain clean data. As in the previous study, OAE data were affected by electrical noise when running on line power (it was not possible to always run with batteries). Data points and/or test conditions contaminated with off-target stimulus levels, poor calibrations, high noise-levels, large differences in noise level between tests, or many unexplained outliers were removed from the data set in an objective fashion, using the same elimination rules across the entire dataset of all volunteers (see footnote 5, Lapsley Miller *et al.*, 2006).

A TEOAE was considered present if its amplitude was greater than the noise floor. A DPOAE was considered present if its amplitude was greater than the noise floor, which was redefined as the average noise floor from the three frequency bins above and below the $2f_1-f_2$ frequency bin plus two standard deviations. For some ears, a pre-test OAE was present, but the post-test OAE was absent. The noise-floor level accompanying an absent post-test OAE was substituted for the absent OAE providing the noise-floor level was lower than the *pre-test* OAE (see Lapsley Miller and Marshall, 2001, pp. 6 and 7; Lapsley Miller *et al.*, 2004, p. 311; and Lapsley Miller *et al.*, 2006, Sec. II E). Thus some OAE changes were potentially underestimated, but this was considered preferable to not using the data at all. The substitution was not done if the post-test noise-floor level was higher than the pre-test OAE, because a high noise-floor level could masquerade as an increase in OAE amplitude. For the susceptibility analyses, it was of interest to know if low or absent OAEs at pre-test increased the chance of STS

TABLE I. The number of ears and the total number of volunteers in each group that contributed to each analysis, listed by the section. The numbers varied at each test frequency, OAE level, and OAE type, because only valid data were used. The exception was for the ANOVAs where volunteers were required to have complete OAE data sets for both ears.

Section and analysis	Group	No. of ears (range)	Total No. of volunteers	Notes
II.A. Volunteers completing study	Noise	570	285	369 noise-exposed volunteers were enrolled, but only 285 completed the study. Not all noise-exposed volunteers were available for post-testing. All control volunteers completed the study.
	Control	64	32	
III.A. ANOVA	Noise	120	60	Ear was a factor in the ANOVAs.
III.B. Forming STS and SES criteria	Control	STS: 64	32	Ears were pooled (Tables II and III).
		SES: 36–54	32	
III.C. Identifying and describing STS and no-STs ears	Noise	STS: 42	36	STSs were detected in 15 left ears only; 15 right ears only; 6 bilateral.
		No-STs: 528	279	
III.D. Identifying and describing SES ears	Noise	SES: 42–49	32–43	The number of ears varied across the left/right ear, frequency and OAE type. There were many ears where SES status could not be determined. Also see Table VI.
		No-SES: 256–398	85–151	
III.E. Comparing STS and SES status	Noise	540	285	See Table V for the SES ears broken down by OAE type and STS status.
III.F. Susceptibility	Noise	STS: 17–21	21	Ear was a factor. The number of ears contributing to the analysis also varied across the OAE type, level, and frequency as all valid data were used.
		No-STs: 217–263	264	
IV.G. Susceptibility for worst ear	Noise	STS: 35–36	36	Ear with the lowest OAE amplitude was used as a predictor.
		No-STs: 234–249	249	
IV.E. Comparison to Lapsley Miller <i>et al.</i> (2006)	Noise	STS: 37–42	36	Ears were pooled.
		No-STs: 439–523	279	

at post-test. Absent pre-test OAEs were estimated where possible by substituting the noise floor for the absent OAE, providing the noise floor was sufficiently low, defined here as being in the tenth percentile of OAE amplitude (see Lapsley Miller *et al.*, 2006, Sec. II E).

To reduce the impact of unusable data, subsets of test frequencies and levels were used in the analyses: TEOAEs at 1, 1.4, 2, 2.8, and 4 kHz, or just the frequencies 2, 2.8, and 4 kHz for some analyses; and DP_{65/45} and DP_{59/50} at 2.5, 2.8, 3.2, 3.6, and 4.0 kHz, or just the frequencies 2.8, 3.2, and 4.0 kHz for some analyses. The TEOAE frequency bands at 0.7 and 5.6 kHz were excluded due to low amplitude resulting from the windowing and filtering used to extract the TEOAE. The DPOAE frequencies 1.8, 2.0, 2.2, and 4.5 kHz were excluded (a) due to electrical noise artifacts that (usually) elevated DPOAE amplitudes and/or noise-floor levels at 2.2 and 4.5 kHz, and (b) for noise-floor levels that were on average much higher than those at 2.5, 2.8, 3.2, 3.6, and 4.0 kHz. It was not possible to sensibly average across the remaining DPOAE frequencies or to compute DPOAE

growth functions due to unusable data. As such, the DP levels DP_{57/45} and DP_{61/55} were not examined further.

We believe that we were measuring permanent changes in audiometric thresholds and OAEs because the post-tests were performed long enough after the noise exposure (three weeks) that any temporary threshold shifts (TTSs) or temporary emission shifts should have resolved. Nevertheless, because it was not possible to confirm the significant audiometric threshold and OAE shifts in individual ears with a follow-up test at a later time, we are careful here to refer to significant threshold shifts (STSs), rather than PTSs, and likewise for OAEs we refer to significant emission shifts (SESs), rather than permanent emissions shifts.

III. RESULTS

Table I provides an overview of the number of volunteers and ears in each group contributing to each analysis. Depending on the analyses, the noise-exposed group is further split into groups of ears with and without STSs (STS

and no-STS) and/or SESs (SES and no-SES). Volunteers may have had unilateral or bilateral significant shifts.

A. Changes in group OAE and audiometric thresholds after noise exposure

Separate repeated-measures analyses of variance (ANOVAs) were conducted on audiometric threshold, TEOAE, and DPOAE data for the subgroup of 60 volunteers (median age 19 years) from the noise-exposed group with complete data sets. A volunteer had a complete data set if, for both ears and for both pre- and post-tests, there was a set of audiometric thresholds (no missing data for any volunteer) and a set of measurable (or estimated) OAEs (TEOAEs at 1, 1.4, 2, 2.8, and 4 kHz; and DP_{65/45} and DP_{59/50} at 2.5, 2.8, 3.2, 3.6, and 4.0 kHz; see Sec. II F). As described earlier, some absent post-test OAEs were estimated using the noise floor. Data from volunteers with incomplete data sets were not used for this analysis. Incomplete data sets were attributable to measurement errors, high noise, and/or absent OAEs at pre-test.⁶ By selecting volunteers with complete data sets, a bias may have been introduced, because those volunteers with unusable data may have lower or absent OAEs from noise-induced damage—the lower OAEs being harder to detect from the noise floor. However, by using complete data sets, comparisons across OAE stimulus types, frequencies, and ears could be made more fairly.

A three-way repeated-measures ANOVA was conducted for audiometric thresholds (test: pre and post; ear: left and right; and frequency: 0.5, 1, 2, 3, 4, and 6 kHz). There was no significant change in audiometric thresholds (main effect) between pre- and post-tests ($F_{1,59}=0.03$, ns). There were, however, significant differences between ears ($F_{1,59}=4.4$, $p<0.05$) and across frequency ($F_{5,295}=14.8$, $p<0.05$). There was also a two-way interaction for test by frequency ($F_{5,295}=3.2$, $p<0.05$). Bonferroni *post hoc t*-test comparisons were used to establish whether any same-frequency pairs contributed to this interaction. The familywise significance level was $p<0.05$, so, for six comparisons, $p<0.008$ was used. None were significant.

A three-way repeated-measures ANOVA was conducted for TEOAE amplitude (test: pre and post; ear: left and right; and frequency: 1, 1.4, 2, 2.8, and 4 kHz). All three factors showed significant main effects. Particularly, there was a 0.94 dB decrease in TEOAE amplitude between pre- and post-testing ($F_{1,59}=14.4$, $p<0.05$). Ears also differed ($F_{1,59}=37.38$, $p<0.05$) as did frequency ($F_{4,236}=14.45$, $p<0.05$). There was one significant two-way interaction: test by frequency ($F_{4,236}=2.9$, $p<0.05$). Bonferroni *post hoc t*-test comparisons were used to establish whether any same-frequency pairs contributed to this interaction. The familywise significance level was $p<0.05$, so, for five comparisons, $p<0.01$ was used. The TEOAE amplitudes at the frequencies 1.4, 2, and 2.8 kHz contributed to the interaction with significant decreases between pre- and post-testing of 1.1, 1.3, and 1.0 dB, respectively.

A four-way repeated-measures ANOVA was conducted for DPOAE amplitude (test: pre and post; ear: left and right; level: stimulus levels of 65/45 and 59/50 dB SPL; and fre-

quency: 2.5, 2.8, 3.2, 3.6, and 4.0 kHz). All four factors showed significant main effects. Particularly, there was a 0.84 dB decrement in DPOAE amplitude between pre- and post-testing ($F_{1,59}=8.6$, $p<0.05$). There were also main effects for ear ($F_{1,59}=4.9$, $p<0.05$), level ($F_{1,59}=140.3$, $p<0.05$), and frequency ($F_{4,236}=68.6$, $p<0.05$). There were three significant two-way interactions: test by level ($F_{1,59}=6.6$, $p<0.05$), ear by level ($F_{1,59}=4.1$, $p<0.05$), and level by frequency ($F_{4,236}=10.7$, $p<0.05$). Bonferroni *post hoc t*-test comparisons were used to establish which levels contributed to the test-by-level, two-way interaction. The familywise significance level was $p<0.05$, so, for two comparisons, $p<0.025$ was used. Neither was significant.

B. Significant threshold shift (STS) and significant emission shift (SES) criteria

Criteria for the detection of STS and SES in individual ears were developed using the same method as in Lapsley Miller *et al.* (2006),⁷ which was based on the standard error of measurement (SE_{meas}) derived from the control-group data. Because the control group of 36 volunteers (64 ears) had not been exposed to noise between tests, the SE_{meas} represents the amount of variability attributable to other sources (i.e., fluctuations in the OAE level over time, differences in probe position or movement, etc.). Any OAE or audiometric threshold in a noise-exposed ear that exceeds these SES or STS criteria can be interpreted as being due to noise exposure (although there is always the possibility of a false positive).

Table II shows the STS criteria. STSs detected at 2, 3, or 4 kHz and the averaged shifts at 2 and 3 kHz, 3 and 4 kHz, and 2, 3, and 4 kHz were used to define the group of STS ears for subsequent analyses. Averaged shifts were included as they are commonly used by regulatory agencies to detect and define threshold shifts. As a crosscheck, no STSs were detected in any ear in the control group. Shifts at 0.5 and 1 kHz were not considered because on their own they are not diagnostic of NIHL, and we were mindful that each look increases the false-positive STS rate. We wanted to focus on those frequencies most likely to show NIHL. Shifts at 6 kHz, however, also were not considered because the STS criterion at 6 kHz was deemed less reliable for detecting noise-induced STS, based on the distribution of negative STSs in the noise-exposed group (there were more negative STS cases than positive).

Table III shows the SES criteria. The criteria for the TEOAEs ranged from approximately 4 to 6 dB, and tended to be smaller than for the DPOAE criteria. The criteria for DP_{59/50} ranged from approximately 6 to 10 dB, and for DP_{65/45} ranged from approximately 7 to 8 dB. The criteria tended to be smaller for the DP_{65/45} compared with DP_{59/50}.

C. STSs detected in the noise-exposed group

A total of 36 out of 285 volunteers in the noise-exposed group (12.6%) were classified with a STS in at least one ear three weeks after the noise exposure (median age 19.1 years). When considering ears rather than volunteers, 42 out of 570 ears (7.4%) were classified with a STS.⁸ There

TABLE II. STS criteria based on the standard error of measurement (SE_{meas}) from the control group (32 volunteers/64 ears) for individual audiometric-threshold frequencies and for averaged frequencies. Shown is the frequency, mean shift between post-testing and pre-testing, SE_{meas} , and the resulting STS criteria (see footnote 7). Note that although the STS criteria were calculated for all frequencies, only frequencies from 2 to 4 kHz and the averaged frequency bands were used to determine the STS status.

Frequency (kHz)	Average shift (dB)	SE_{meas} (dB)	STS (dB)
0.5	-1.4	4.0	20
1	-1.8	3.6	15
2	-2.0	3.4	15
3	-2.3	3.6	15
4	-2.0	3.9	15
6	-1.5	4.5	20
Mean 2 and 3	-2.2	3.1	10
Mean 3 and 4	-2.2	3.1	10
Mean 2, 3, and 4	-2.1	2.7	8.3

were 15 left STS ears, 15 right STS ears, and 6 bilateral STS ears. Table IV summarizes the STS and no-STS ears by left and right ears.

Figure 1 shows the average pre- and post-test audiograms for the STS ears (42 ears) compared with the no-STS ears (528 ears). The STS ears' average thresholds increased while the no-STS ears' average thresholds stayed the same. Although there were the same number of left STS ears and right STS ears, the left ear STSs on average were larger and broader-band than the right ear STSs. The largest average increases in threshold were 13.3 dB at 4 kHz for the right ears and 11.7 dB at 4 kHz for the left ears. The largest individual increases in threshold were 40 dB STSs at 4 kHz in both ears of one volunteer.

D. SESs detected in the noise-exposed group

SES status was determined for each ear of each volunteer in the noise-exposed group, separately for each OAE

TABLE III. SES criteria based on the standard error of measurement (SE_{meas}) from the control group (32 volunteers/64 ears). Shown are the OAE type, f_2 frequency for DPOAEs or half-octave frequency band for TEOAEs, the number of ears contributing to the calculation, SE_{meas} , and the resulting SES criteria (see footnote 7). Note that although the SES criteria were calculated for all valid frequencies, only some frequencies were used to determine the SES status (2.5, 3.2, and 4 kHz for DPOAEs, and 2, 2.8, and 4 kHz for TEOAEs).

OAE type	Frequency (kHz)	Ears	SE_{meas} (dB)	SES (dB)
DP _{59/50}	2.5	40	2.0	6.0
	2.8	40	2.5	7.6
	3.2	48	3.3	9.9
	3.6	45	2.8	8.5
	4.0	51	2.9	8.7
DP _{65/45}	2.5	44	2.5	7.5
	2.8	48	2.5	7.5
	3.2	54	2.6	7.7
	3.6	54	2.3	7.0
	4.0	54	2.2	6.7
TEOAE	1.0	45	2.0	5.8
	1.4	48	2.0	6.0
	2.0	43	2.0	6.1
	2.8	42	1.7	5.2
	4.0	36	1.3	4.0

type. For comparison with the three frequencies used to assess STS, three frequencies/frequency bands were considered for each OAE type within the 2–4 kHz range. For TEOAEs, this was 2, 2.8, and 4 kHz half-octave bands. For DPOAEs this was 2.5, 3.2, and 4.0 kHz.⁹ Three types of SES status were defined.

- *No-SES*. No OAE decrements at any of the three frequencies.
- *SES*. At least one significant decrease in OAE amplitude at any of the three frequencies. Other frequencies could have either no shifts or unusable data.
- *Unknown-SES*. At least one frequency band where SES status could not be determined¹⁰ and no SES shifts at the other frequencies. In other words, it was unknown whether the ear should be a no-SES or a SES. No distinction is made here between OAEs below the noise-floor criterion and data loss due to measurement problems.

Summarizing from Table IV, which provides a breakdown of SES status by ear and OAE type, 42 out of 285 noise-exposed group volunteers (14.7%) showed a DP_{59/50} SES, 32 volunteers (11.2%) showed a DP_{65/45} SES, and 43 volunteers (15.1%) showed a TEOAE SES. This included two, ten, and six volunteers with bilateral SES, for each OAE type, respectively. When considering ears rather than volunteers, 44 out of 570 noise-exposed ears (7.7%) showed a DP_{59/50} SES, 42 ears (7.4%) showed a DP_{65/45} SES, and 49 ears (8.6%) showed a TEOAE SES. These percentages are similar to those seen for STS, but are underestimated due to the large number of ears with unknown-SES status. The true SES rate is likely to be much higher.¹¹

To estimate the true SES rate (for individual frequencies), the percentages were recalculated (separately for each OAE type) for the group of volunteers where status was known for both ears (see Table IV). For these subgroups, 28 out of 158 volunteers (17.7%) showed a DP_{59/50} SES, 29 out of 180 volunteers (16.1%) showed a DP_{65/45} SES, and 28 out of 113 volunteers (24.8%) showed a TEOAE SES. When considering ears rather than volunteers, 30 out of 316 ears (9.5%) showed a DP_{59/50} SES, 39 out of 360 ears (10.8%) showed a DP_{65/45} SES, and 34 out of 226 ears (15.0%) showed a TEOAE SES. There was a tendency for more left

TABLE IV. Breakdown of the 285 volunteers in the noise-exposed group by STS status and SES status for the left/right ear and the measurement type. The first number is the count, and the number in parentheses is the overall percentage. The Unknown category represents those ears for which a SES determination could not be made, usually due to unusable data. See text for summaries of STS and SES rates for volunteers and ears.

Audiometric thresholds			Right ears		
			STS	No-STS	Unknown
Left ears	STS		6 (2)	15 (5)	0 (0)
	No-STS		15 (5)	249 (87)	0 (0)
	Unknown		0 (0)	0 (0)	0 (0)
DP _{59/50}			Right ears		
			SES	No-SES	Unknown
Left ears	SES		2 (1)	10 (4)	6 (2)
	No-SES		16 (6)	130 (46)	39 (14)
	Unknown		8 (3)	32 (11)	42 (15)
DP _{65/45}			Right ears		
			SES	No-SES	Unknown
Left ears	SES		10 (4)	5 (2)	1 (0)
	No-SES		14 (5)	151 (53)	41 (14)
	Unknown		2 (1)	36 (13)	25 (9)
TEOAE			Right ears		
			SES	No-SES	Unknown
Left ears	SES		6 (2)	15 (5)	7 (2)
	No-SES		7 (2)	85 (30)	26 (9)
	Unknown		8 (3)	38 (13)	93 (33)

ears to show DP SESs (~61% left ears and ~39% right ears) and for more right ears to show TEOAE SESs (38% left ears and 62% right ears).

Figures 2–4 show the average pre- and post-test OAE amplitudes for the SES ears compared with the no-SES ears, by left and right ears for each OAE type, without regard to

STS status. Error bars are 95% confidence intervals. Note that SES status was determined from only three frequencies for each OAE type. To maximize the amount of data going into each point, there was no requirement for an ear to have

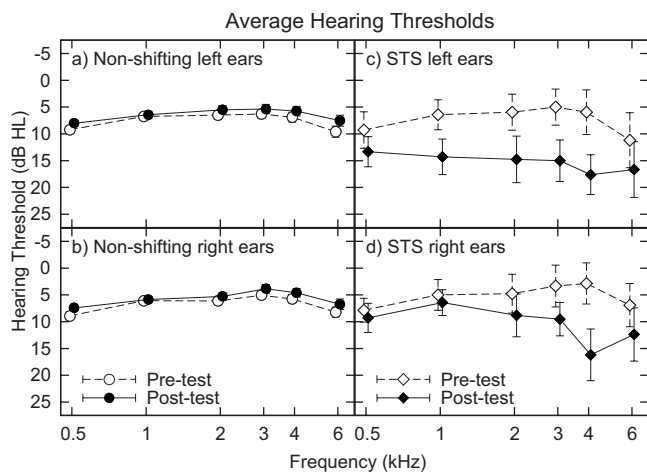


FIG. 1. Average pre-test and post-test audiometric thresholds for the noise-exposed group by STS status. Average pre-test thresholds for the 42 STS ears (21 left and 21 right ears) were essentially the same as for the 528 no-STS ears (286 left ears and 286 right ears). Post-test audiograms show that the average thresholds for the STS ears increased up to 13.3 dB (left ears, 4 kHz), while the no-STS ears stayed essentially the same. The error bars are 95% confidence intervals.

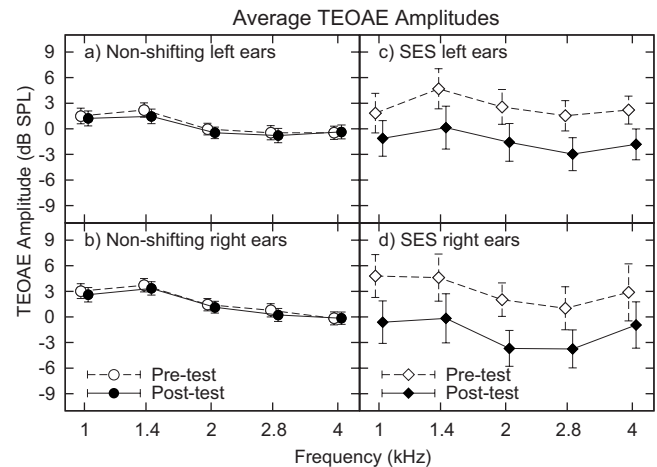


FIG. 2. Average pre-test and post-test TEOAE amplitudes for the noise-exposed group by significant TEOAE shift (SES) status. Average pre-test amplitudes for the SES ears (22–27 left ears and 14–21 right ears) were slightly higher than for the no-SES ears (112–118 left ears and 129–138 right ears). Average post-test TEOAE amplitudes decreased by approximately 4 dB from pre-test for the SES ears, while the post-test average for the no-SES ears stayed essentially the same. The error bars are 95% confidence intervals. The number of ears contributing to the average at each frequency varied because of some unusable data.

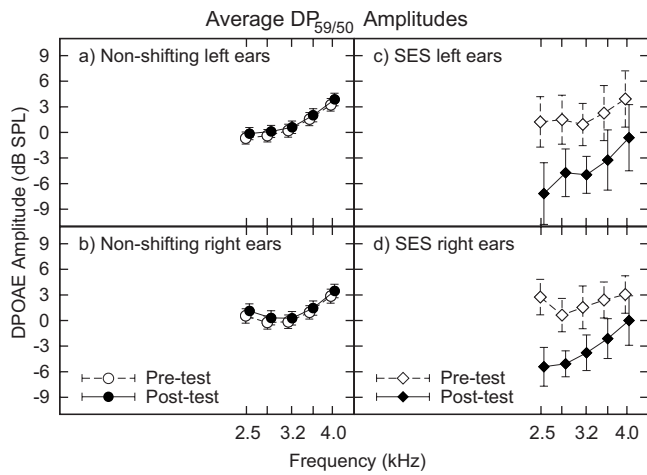


FIG. 3. Average pre-test and post-test $DP_{59/50}$ amplitudes for the noise-exposed group by significant $DP_{59/50}$ shift (SES) status. Average pre-test amplitudes for the SES ears (16–17 left ears and 25–26 right ears) were slightly higher than the average for the no-SES ears (180–185 left ears and 166–172 right ears). Average post-test $DP_{59/50}$ amplitudes decreased by approximately 6 dB from pre-test for the SES ears, while the post-test average for the no-SES ears stayed essentially the same. The error bars are 95% confidence intervals. The number of ears contributing to the average at each frequency varied because of some unusable data.

usable data at all displayed frequencies; however, an ear needed both a valid pre- and post-test measurement at a frequency to be included. There were more unusable data for the SES ears because these ears needed only one SES at one frequency to be considered a SES ear, whereas the no-SES ears were required to have no SESs at all three frequencies.

The SES ears showed on average an ~ 4 dB broadband TEOAE decrement and ~ 6 dB DPOAE decrements across 2.5–4 kHz in average OAE amplitude between pre- and post-testing, whereas the no-SES ears showed essentially no change. There was a tendency, especially for TEOAEs, for

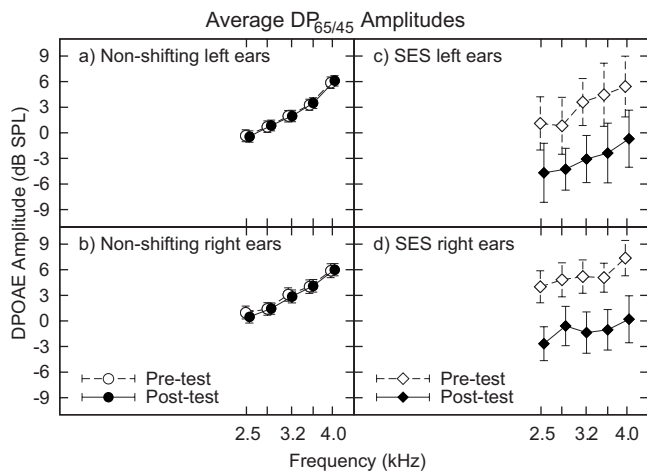


FIG. 4. Average pre-test and post-test $DP_{65/45}$ amplitudes for the noise-exposed group by significant $DP_{65/45}$ shift (SES) status. Average pre-test amplitudes for the SES ears (15–16 left ears and 24–26 right ears) were slightly higher than the average for the no-SES ears (201–206 left ears and 188–192 right ears). Average post-test $DP_{65/45}$ amplitudes decreased by approximately 6 dB from pre-test for the SES ears, while the post-test average for the no-SES ears stayed essentially the same. The error bars are 95% confidence intervals. The number of ears contributing to the average at each frequency varied because of some unusable data.

average pre-test amplitudes to be higher for the SES ears compared with the no-SES ears, but this may be due solely to the small N . In general, these graphs indicate that the method used to determine the SES status was appropriate.

E. Comparison of STS and SES

Table V shows the resulting 2×3 matrices for the STS and no-STS ear versus the SES, no-SES, and unknown-SES ears. The amount of data is small in some cells, and is also unevenly balanced, so it is important to not overinterpret the findings. The count of the SES ears is likely to be an underestimate. First, many potential SES ears are in the unknown-SES category because the SES is masked by noisy measurements. Second, ears with low-level or absent OAEs at pre-test cannot show a SES at post-test; these ears are examined in more detail in Sec. III F.

The nonparametric phi coefficient (Siegel, 1956) was used as a measure of association for the 2×2 matrices to determine whether STSs and SESs tended to occur together in the same ear (the unknown-SES category was not included). The phi coefficient can be interpreted similarly to a correlation coefficient and can be used for small data sets. Coefficients below 0.35 are considered to indicate no more than trivial associations (Fleiss *et al.*, 2003). There was essentially no association between the STS status and the SES status for TEOAEs (left ears, $\phi=0.25$; right ears, $\phi=0.22$), $DP_{65/45}$ (left ears, $\phi=0.11$; right ears, $\phi=0.10$), or $DP_{59/50}$ (left ears, $\phi=0.18$; right ears, $\phi=0.02$).

To further assess whether STSs and SESs were associated, conditional probabilities were considered for the ears in Table V. As shown in Table VI, in general, the probability (P) of a SES in an ear was higher than the probability of a STS. Further, $P(\text{STS}|\text{SES})$, which is the conditional probability of the STS in the subgroup of the SES ears, was higher than the $P(\text{STS})$, which is the STS base rate, indicating that STS ears were overrepresented among the SES ears. Going the other way, $P(\text{SES}|\text{STS})$ which is the conditional probability of the SES in the subgroup of the STS ears, was higher than $P(\text{SES})$, which is the SES base rate, indicating that SES ears were overrepresented among the STS ears. In the STS ears, TEOAEs tended to show SES more than did DPOAEs. Because of the small numbers in some of the cells, any further analysis would be inappropriate.

F. OAE predictors of susceptibility to NIHL

Pre-test OAE amplitudes were used as predictors of the STS status in the noise-exposed ears.¹² There were two groups of interest: the 42 STS ears and the 528 no-STS ears. Due to potential differences in the NIHL susceptibility in the left and right ears, they were kept separated in the analyses. As described earlier, where possible, pre-test OAE amplitudes below the noise floor were estimated with the noise-floor level, providing the noise floor was sufficiently low. Between 17 and 21 STS ears and 217–263 no-STS ears contributed to the analysis for each frequency, OAE type, and ear.

The positive predictive value (PPV) (Zhou *et al.*, 2002) is the conditional probability of an ear from the noise-

TABLE V. STS vs SES matrices. The first number is the count, and the number in parentheses is the overall percentage. For the left and right ears separately, ears were grouped by whether they were classified as STS and/or SES ears. The unknown-SES category is for those ears where there were unusable data; these ears were not used in the analysis of the matrices.

OAE type	STS status	SES status					
		Left ear			Right ear		
		No-SES	SES	Unknown-SES	No-SES	SES	Unknown-SES
DP _{59/50}	No-STS	174 (61)	14 (5)	76 (27)	161 (56)	24 (8)	79 (28)
	STS	11 (4)	4 (1)	6 (2)	11 (4)	2 (1)	8 (3)
DP _{65/45}	No-STS	191 (67)	13 (5)	60 (21)	178 (62)	22 (8)	64 (22)
	STS	15 (5)	3 (1)	3 (1)	14 (5)	4 (1)	3 (1)
TEOAE	No-STS	111 (39)	21 (7)	132 (46)	130 (46)	16 (6)	118 (41)
	STS	7 (2)	7 (2)	7 (2)	8 (3)	5 (2)	8 (3)

exposed group *with* STS after basic training, *given* a test result of a low-level OAE. A low-level OAE is defined as an OAE amplitude that is less than a cutoff value. By varying the cutoff value over the entire range of OAE amplitudes, the entire PPV function may be generated. Once the entire PPV function is known, an optimal cutoff point may be chosen to define a “low-level” OAE (which may vary depending on the purpose, and the outcomes associated with the diagnosis). The PPV is also known as the *a posteriori* conditional probability: $P(\text{STS}|\text{OAE} \leq \text{cutoff})$.

Figure 5 shows the PPV as a function of OAE amplitude for each ear, OAE type, and frequency. Without knowledge of the OAE level in a given ear, there was a probability of around 0.07–0.08 that the ear would be classified with STS. With knowledge of the OAE level, the probability an ear would be classified with STS rose to a maximum of 0.67, indicating an eight- to ninefold increased risk for STS. TEOAEs at 2.8 and 4 kHz tended to be better predictors for the left ears, with OAE amplitudes below approximately –5 dB SPL indicating an increased risk for STS. DPOAEs at 4 kHz tended to be better predictors for the right ears, with OAE amplitudes below approximately –5 to –10 dB SPL indicating an increased risk for STS. To summarize the risk,

Table VII provides the maximum increased risk (maximum PPV/base-rate over the OAE amplitude) across all OAE types by frequency.

To relate these figures to the percentage of volunteers at increased risk, the PPV functions are replotted in Fig. 6 for each ear and each OAE type at 4 kHz after transforming OAE amplitudes into percentiles. For the left ear (but not the right ear), TEOAEs at 4 kHz show an increased risk for STS in the bottom quartile, whereas for the left ear (but not the right ear), DPOAEs at 4 kHz show an increased risk for STS in the bottom decile.

G. Susceptibility to NIHL for volunteers rather than ears using “worst ear” as a predictor

In a clinical situation, the focus is more on the risk of STS for an individual person, rather than individual ears. One way to use the information from both ears is to take the results from the worst ear (the ear with the lowest OAE amplitude) and use that as the predictor for the STS risk. Figure 7 shows the results of such an analysis for the two best DP frequencies and the three best TEOAE frequencies. For each noise-exposed volunteer and for each OAE type

TABLE VI. STS ears are over-represented in the group of SES ears, compared with the probability (P) of a STS in general. Likewise SES ears are over-represented in the group of STS ears, compared with the probability of a SES in general. This finding holds over the left and right ears and for all three OAE types, except for DP_{59/50} in the right ears, where representation was proportional, and where OAEs had the highest variability. The pooled category represents the results pooled over the ear and the OAE type. The true SES rate is underestimated because there are likely to be some unidentified SES ears in the large group of unknown-SES ears, where SES status could not be determined at all three frequencies. (For the underlying cell counts, see Table V.)

OAE type	Ear	$P(\text{STS})$	$P(\text{STS} \text{SES})$	STS represented in SES group	$P(\text{SES})$	$P(\text{SES} \text{STS})$	SES represented in STS group	$P(\text{unknown-SES})$
DP _{59/50}	Left	0.07	0.22	Over	0.09	0.27	Over	0.29
	Right	0.07	0.08	Proportionally	0.13	0.15	Proportionally	0.31
DP _{65/45}	Left	0.08	0.19	Over	0.07	0.17	Over	0.22
	Right	0.08	0.15	Over	0.12	0.22	Over	0.24
TEOAE	Left	0.10	0.25	Over	0.19	0.50	Over	0.49
	Right	0.08	0.24	Over	0.13	0.38	Over	0.44
Pooled		0.08	0.19	Over	0.12	0.27	Over	0.33

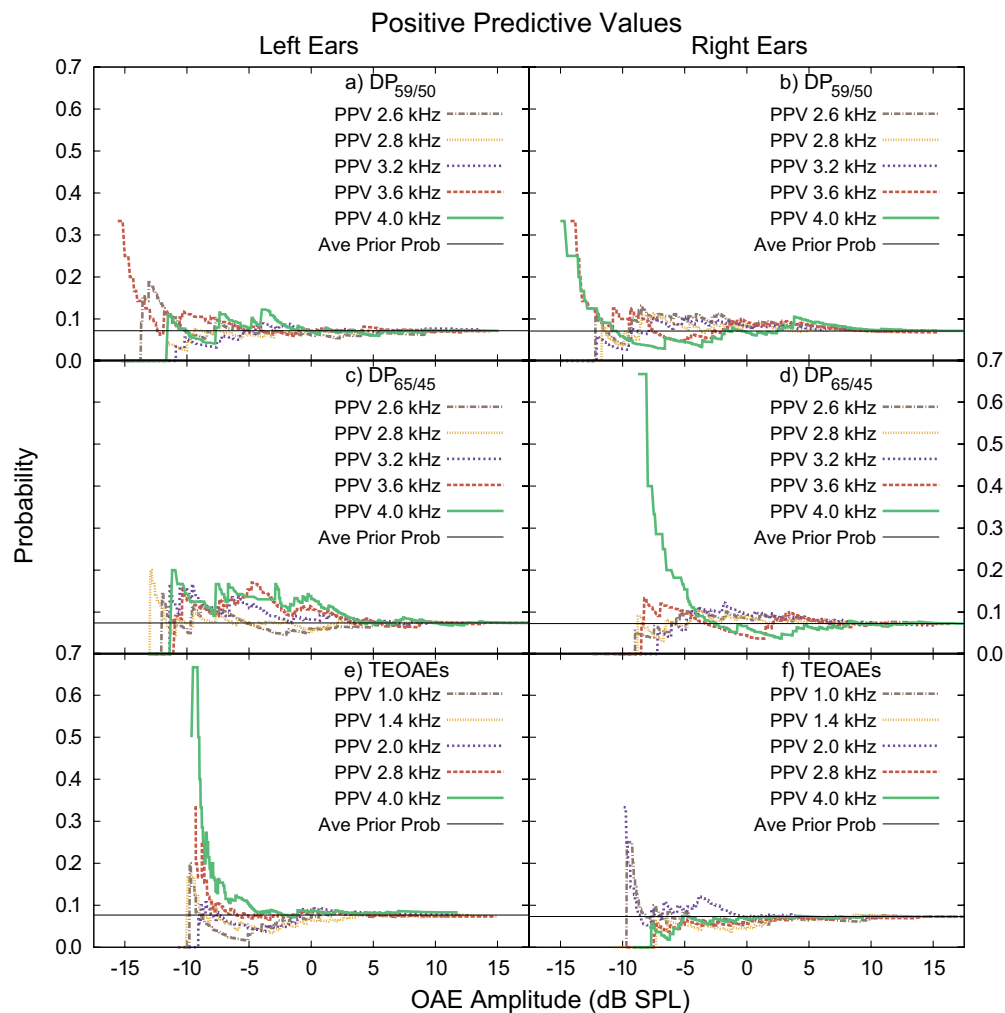


FIG. 5. (Color online) PPV, for the left and right ears separately, as a function of the PPV criterion, which is OAE amplitude (in dB SPL). PPV is the probability that an ear was classified with a STS given an OAE amplitude less than the criterion. As the OAE amplitude decreased, PPV tended to increase for the higher-frequency bands, but not for all OAE types and frequencies. [(a) and (b)] $DP_{59/50}$, [(c) and (d)] $DP_{65/45}$, and [(e) and (f)] TEOAEs. The thin solid horizontal line represents the prior probability of a STS averaged over the displayed frequencies.

and frequency, the lowest OAE amplitude of the two ears was chosen, or if there were valid data for only one ear then that ear constituted the worst ear. If there were no valid data for either ear, the volunteer was not included in the analysis at that test point. Note that unlike the analyses so far, the contralateral ears of the 30 volunteers with unilateral STS were included with the STS ears rather than with the no-STS ears (in the cases where that ear had the lowest OAE amplitude). When choosing the worst ear, TEOAEs, especially at 4 kHz, were the best predictor of incipient NIHL.

IV. DISCUSSION

A. OAEs are more sensitive than audiometric thresholds to noise exposure

The repeated-measures ANOVA indicated that OAEs were more sensitive to noise-induced changes to the inner ear than were audiometric thresholds. Both DPOAEs and TEOAEs showed significant decreases in OAE levels after the noise exposure, but there was no change in audiometric thresholds for the subgroup of 60 noise-exposed volunteers with complete data sets. The 2×2 matrices for SES versus

TABLE VII. Maximum increased risk for STS (PPV/base-rate) for each OAE type and frequency, by ear. Each number represents how many times more likely a STS is given a low pre-test OAE result relative to the base rate.

OAE type	Frequency (kHz)	Maximum increased risk	
		Left ears	Right ears
$DP_{59/50}$	2.5	2.6	1.8
	2.8	1.1	1.6
	3.2	1.2	1.5
	3.6	4.7	4.9
	4.0	1.7	4.7
$DP_{65/45}$	2.5	1.9	1.4
	2.8	2.7	1.4
	3.2	2.3	1.7
	3.6	2.3	1.9
	4.0	2.7	9.2
TEOAE	1.0	2.6	3.4
	1.4	2.2	1.1
	2.0	1.4	4.4
	2.8	4.6	1.0
	4.0	8.1	1.0

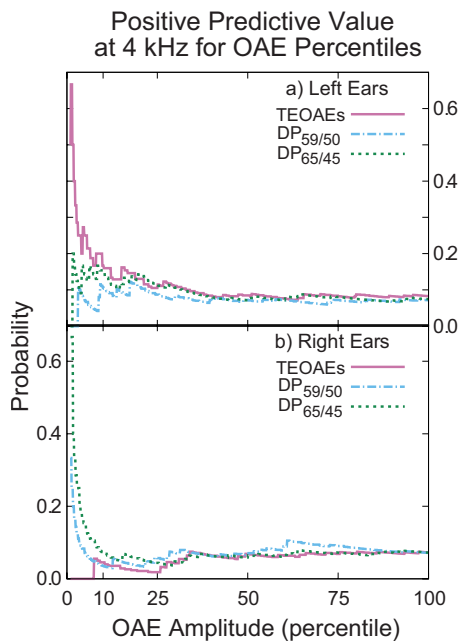


FIG. 6. (Color online) PPV at 4 kHz (from Fig. 5), for the left and right ears separately, for each OAE type replotted as a function of OAE amplitude in percentiles.

STS status indicated a higher SES rate compared with the STS rate in the noise-exposed ears, and there was a tendency for the STS ears to also have SESs and for SES ears to also have STSs. TEOAE SES status showed more consistency with the STS status than with the DPOAEs, despite the larger amount of unusable data with the TEOAEs. These findings are consistent with Lapsley Miller *et al.* (2006), where the same experimental protocol was used, and with many other longitudinal studies that also showed changes in OAEs without accompanying changes in audiometric thresholds (Engdahl *et al.*, 1996; Murray *et al.*, 1998; Murray and LePage, 2002; Konopka *et al.*, 2005; Seixas *et al.*, 2005a; Duvdevany and Furst, 2006).

These results could be due to on-frequency inner-ear damage in the 2–4 kHz range that causes subclinical changes insufficient to affect audiometric thresholds but to which OAEs are sensitive. This is consistent with observations in animals that damage to outer hair cells (OHCs) can be extensive with no concomitant change in audiometric thresholds (Hamernik *et al.*, 1989; Hamernik *et al.*, 1996), and consistent with the theory that there is OHC redundancy (LePage *et al.*, 1993), where it is thought that there are many more OHCs than what is required for normal hearing. The OHC loss therefore shows up in OAE measurements before audiometric threshold measurements because OAE measurements more directly measure OHC activity. Alternatively, the results could be due to unmeasured higher-frequency inner-ear damage (that may or may not affect high-frequency hearing thresholds) that affects OAEs measured at lower frequencies, but not audiometric thresholds at those lower frequencies. This higher-frequency damage might influence the transmission of a lower-frequency OAE out to the middle ear (Lonsbury-Martin and Martin, 2007). Furthermore, with some OAE stimulus configurations (containing high-frequency energy), high-frequency damage could lessen the

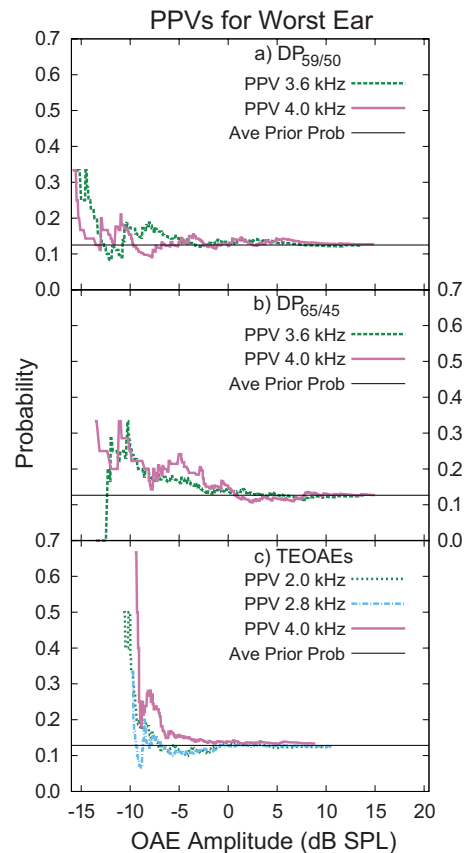


FIG. 7. (Color online) PPVs as a function of PPV criterion, which in this case is OAE amplitude for the worst ear, which is the way it would be implemented in occupational audiology programs. For each volunteer, the ear with the lowest OAE amplitude was used as the predictor. (a) $DP_{59/50}$ at 3.6 and 4 kHz, (b) $DP_{65/45}$ at 3.6 and 4 kHz and (c) TEOAEs at 2, 2.8, and 4 kHz. The thin solid horizontal line represents the prior probability of a STS averaged over the displayed frequencies.

distortion-component OAE from the high-frequency place that creates a lower-frequency stimulus-frequency OAE (SFOAE),¹³ which can interact with OAEs generated at that lower frequency. It was not possible in the current study to measure high-frequency hearing thresholds or high-frequency OAEs, making it difficult to disentangle the two theories; however, the results of others offer some clues.

For DPOAEs in humans, diminished OAE amplitudes without an accompanying hearing loss in the same frequency region have been associated with a hearing loss at higher frequencies (Arnold *et al.*, 1999; Dorn *et al.*, 1999). Arnold *et al.* (1999) used 50 subjects, the majority of whom were males, with normal hearing (<20 dB HL from 0.25 to 8 kHz) and ages from 17 to 37 years. They reported minimal noise exposure, but people, particularly males, living in modern civilizations do tend to accumulate damage from noise exposure. The multivariate analyses of Dorn *et al.* (1999) included hundreds of subjects, age 1–96 years, and hearing levels from –5 to 120 dB HL at 0.75–8 kHz. In contrast, Schmuziger *et al.* (2005) minimized the effects of previous noise exposure by using younger subjects (age 16–19 years), and fewer males (38%) in the group (all with normal hearing, as well as reports of minimal previous noise exposure). The high-frequency (8–16 kHz) thresholds for this group were only minimally related to lower-frequency

DPOAEs. In rodents, [Withnell and Lodde \(2006\)](#) did not see lower-frequency DPOAE amplitude losses when higher-frequency regions were damaged by noise. These results suggest that the more likely explanation for the influence of high-frequency thresholds on much lower-frequency DPOAEs is subclinical damage at the lower frequency.

For TEOAEs in humans, decreased OAE amplitudes without an accompanying audiometric-threshold decrement in the same-frequency region also were associated with a hearing loss at higher frequencies ([Avan et al., 1997](#); [Konopka et al., 2005](#)). The subjects of [Avan et al. \(1997\)](#) (nearly half of whom were males) had normal hearing up to 4 kHz, and were older—ages 24–54 years. The group from [Konopka et al. \(2005\)](#) consisted of 92 young, male, noise-exposed soldiers. In a young population with less noise exposure, and with normal hearing up to 8 kHz, high-frequency (8–16 kHz) thresholds were not related to lower-frequency TEOAEs ([Schmuziger et al., 2005](#)).

[Yates and Withnell \(1999\)](#), using a novel measurement technique that allowed the measurement of high-frequency TEOAEs, observed that TEOAEs evoked by a high-pass click included frequencies lower than those in the stimulus in guinea pigs. The generation of new frequencies that were not present in the stimulus implies that the OAEs were generated from a distortion mechanism; these OAEs also act as a stimulus that elicits reflection-component SFOAEs at lower frequencies. After noise exposure, which damaged the high-frequency region in guinea pigs, lowered TEOAE amplitudes were found not only at the higher frequency where the eighth-nerve compound-action-potential (CAP) thresholds were lowered, but also at lower frequencies where the CAP thresholds were not lowered ([Withnell et al., 2000](#)). In humans, however, not only is the distortion mechanism relatively smaller than it is in guinea pigs ([Shera and Guinan, 1999](#)), but the method used for clinical TEOAE measurements windows out the first few milliseconds of the TEOAE to reduce stimulus artifact ([Bray and Kemp, 1987](#)). This leaves only the TEOAE reflection component ([Knight and Kemp, 1999](#); [Kalluri and Shera, 2007](#); [Sisto et al., 2007](#); [Withnell et al., 2008](#)). Furthermore, behavioral thresholds at ultrahigh frequencies would not influence most TEOAE measurements with humans because the TEOAE stimulus usually does not have much energy above 5 kHz. With a TEOAE stimulus that extends up to 5 kHz, the TEOAE and SFOAE spectra in individual ears are nearly identical, at least up to 2.4 kHz, implying that with TEOAEs, the lower-frequency SFOAE that gets generated due to the higher-frequency distortion component does not have much effect on the lower-frequency SFOAE that is solely generated from that place (e.g., [Kalluri and Shera, 2007](#)). The results from these TEOAE studies also suggest that on-frequency subclinical damage is the predominant reason why OAE amplitudes can decrease when hearing levels remain unchanged in humans.

Studies that have shown TEOAE decrements in individual ears to be broader than DPOAE decrements may be indicative of TEOAEs being more sensitive to subclinical damage than DPOAEs (e.g., [Lapsley Miller et al., 2004](#); [Lapsley Miller et al., 2006](#)), consistent with [Shera's \(2004\)](#)

view that the reflection component should be more sensitive to noise damage. TEOAEs as we typically measure them are primarily reflection mechanism, and DPOAEs are a mix of the two mechanisms. Therefore, it is not surprising that DPOAEs and TEOAEs often are equally sensitive for groups, but TEOAEs tend to edge out DPOAEs in sensitivity for individual ears.¹⁴

There are some studies that do not show OAEs as being more sensitive than audiometric thresholds. [Lapsley Miller et al. \(2006\)](#) found significant changes in group audiometric thresholds along with changes in OAEs, but there was little consistency between changes in thresholds and OAEs in individual ears. [Duvdevany and Furst \(2007\)](#) measured hearing and TEOAEs in the same individuals annually three times—neither hearing nor TEOAEs changed in the second year, but both did in the third year. Their TEOAE stimulus was 84 dB pSPL, which would not be maximally sensitive to noise damage.¹⁵

Aging and sex differences can be discounted in the current study because all the participants were young men and the study duration of 13 weeks was too short for aging to have any measurable impact. Nor is audiometric resolution an explanation for the greater sensitivity of OAEs to noise-induced changes in the inner ear. The standard clinical protocol, which produces a resolution of 5 dB, may hinder the detection of small changes in audiometric thresholds, even in the group average. However, if the only reason for the difference between OAEs and audiometric thresholds is resolution, all the STS ears that were identified should also show SESs, but this was not the case. Even within the subset of ears with both SESs and STSs, there was not much consistency across frequency and OAE type (results not reported here in detail).

The typical finding for the STS ears was either an accompanying SES (not necessarily across all OAE types) or low-level or absent OAEs. For a couple of ears where there was STS but no SES and normal OAEs, the STS was small and possibly a false positive (it was not possible to do a confirmation audiogram).

B. STS and SES criteria

The SE_{meas} values underlying the STS criteria were smaller here than in [Lapsley Miller et al. \(2006\)](#), perhaps because the current study used double-walled sound-attenuating chambers, whereas the earlier study used single-walled chambers in a noisier shipboard environment. The current STS criteria were identical to those developed in [Lapsley Miller et al. \(2004\)](#), where the testing environment was similar.

If possible, it is important to derive STS (and SES) criteria from a control group tested in the same environment so that there is some certainty that the shifts are significantly different from test-retest variability. For instance, in the current study, using all the derived STS criteria (Table II), STS was detected in 36 noise-exposed volunteers (42 ears) or 12.6% of volunteers (7.4% of ears). If the strict clinical criterion that is commonly used by regulatory agencies was used instead, which is an average shift at 2, 3, and 4 kHz of

at least 10 dB (Mining Safety and Health Administration, 1999; Department of Defense, 2004; Federal Railroad Administration, 2006; Occupational Safety & Health Administration, 2007), STS would have been detected in only 17 volunteers (18 ears) or 5.9% of volunteers (3.2% of ears). The opposite can also happen, where the criteria chosen are too lax. For instance, if someone arbitrarily chose a STS criterion of a 10 dB shift at any single frequency (without any reference to a control group), in our current study STS would have been detected in 87 volunteers (109 ears) or 30% of volunteers (19.1% of ears). Most of these shifts are false-positive STSs because the criterion was less than the test-retest variability.

The detection of a STS does not necessarily mean the ear had a hearing loss as there is a chance that the STS was a false positive. An upper limit for our false-positive rate (for STS at three single frequencies and three averaged frequencies; assuming independence of frequencies) is approximately 11% (for both positive and negative STSs). The probability of a false positive across six frequencies is one minus the probability of no false positives at any frequency. Because our STS criteria were based on a 98% confidence interval (see footnote 7), this is $1 - 0.98^6$. The actual false-positive rate is likely to be lower because (a) we looked only at positive STS, so the false-positive rate would be only 5.5% at most, (b) the frequencies are correlated, and (c) the 5 dB resolution of the audiogram meant that we rounded up the raw criteria based on multiples of the SE_{meas} to the next largest available step so the probability of a false positive at each frequency was lower. This is borne out when applying the STS criteria to the control group where there were no STSs detected. In the larger noise-exposed group, however, we would expect some of the STSs to be false positives, and indeed there are some shifts that are not compelling from a clinical viewpoint (e.g., a shift only at 2 kHz). A stricter STS criterion, however, would have meant missing more true STSs. It was unfortunate that the recruits' schedule did not allow time for immediate retesting of STSs, which would have decreased the false-positive rate.

NIOSH (National Institute for Occupational Safety and Health, 1998) suggested a different STS criterion—a 15 dB shift at any tested frequency (0.5, 1, 2, 3, 4, 6, or 8 kHz), with an immediate retest being optional. ASHA (American Speech-Language-Hearing Association, 1994) also suggested a significant change criterion (for monitoring ototoxic hearing loss) greater than 15 dB at any one frequency or greater than or equal to 10 dB at two or more adjacent frequencies. The current study, as well as previous ones (e.g., Marshall and Hanna, 1989; Lapsley Miller *et al.*, 2004) found that the SE_{meas} at a single frequency varies as a function of frequency, with lower and higher frequencies having a larger SE_{meas} . Shaw (1966) demonstrated that supra-aural earphone-placement variations have the largest effect at these frequencies. For our data, the NIOSH criterion was the same as ours at 1–4 kHz (National Institute for Occupational Safety and Health, 1998), but too lax at 0.5 and 6 kHz. The ASHA criterion was too strict for 1–4 kHz, but applicable above and below that, as well as for the 10 dB two-frequency average criterion.

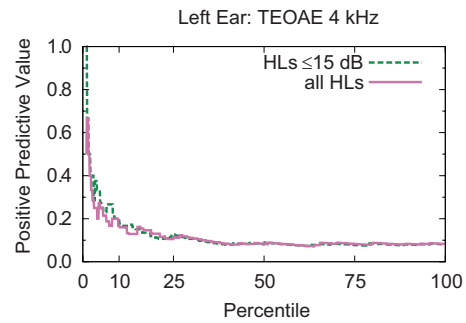


FIG. 8. (Color online) PPV as a function of OAE amplitude in percentiles for TEOAEs at 4 kHz for the left ears from Fig. 6 (solid line) compared with the same data after excluding ears with audiometric thresholds >15 dB HL (dashed line).

The NIOSH suggestion of retesting immediately following a STS is a good one. For example, in the current study, we estimated an upper bound for the false-positive STS rate to be 5.5%. If a STS is retested, then we would expect the STS rate to diminish to 0.5% (probability of a STS over six frequencies multiplied by the probability of a STS at one frequency, 0.055×0.01 ; assuming only positive STSs are of interest). Basing the STS criterion on the known test-retest reliability of a test situation is necessary for control of false-positive STSs. Our STSs are a better estimate of true STS than may be the case when arbitrary values are chosen.

The SE_{meas} values underlying the TEOAE SES criteria were similar to Lapsley Miller *et al.* (2004), but were slightly larger than in Lapsley Miller *et al.* (2006), where the equipment was run on battery power more often, which tended to produce a lower noise floor. The SE_{meas} values underlying the DPOAE SES criteria were also slightly larger than in Lapsley Miller *et al.* (2006), but could not be directly compared to Lapsley Miller *et al.* (2004) because here they were based on measurements at individual frequencies, rather than averaged within half-octave bands. In general, the SE_{meas} values were mostly comparable to those reported elsewhere (Franklin *et al.*, 1992; Beattie and Bleech, 2000; Beattie, 2003; Seixas *et al.*, 2005b; Wagner *et al.*, 2008).

C. Susceptibility to NIHL from impulse noise

In the analyses discussed so far, all ears used had pre-test OAE amplitudes that were measurable. Many of the ears that ended up in the unknown-SES category had OAE signal-to-noise ratios that did not meet the criteria for presence. The second thrust of the analyses showed that low-level pre-test OAE amplitudes were predictive of subsequent STS status for some OAE types, frequencies, and left and right ears (Fig. 5). The increased risk of a STS for those ears with low pre-test OAE levels cannot be explained by pre-test audiometric-threshold differences between the STS ears and the no-STS ears as there was essentially no difference between pre-test audiometric thresholds for these groups, as shown in Fig. 1. To further illustrate this point, the analysis underlying Fig. 6 for TEOAEs at 4 kHz, for left ears, was rerun after excluding all ears with audiometric thresholds >15 dB HL at 4 kHz (see Fig. 8). Seventeen no-STS ears and zero STS ears were excluded using this new criterion.

The exclusion of these ears only enhances the finding that pre-test OAE levels can be predictive of subsequent STS. This is supported by an animal study by [Perez et al. \(2004\)](#) that showed that ears with existing hearing loss were less likely to get further hearing loss. This implies that ears with low-level OAEs and hearing loss would be less likely to get further hearing loss. It is those ears with low-level OAEs and normal hearing that are at risk.

The OHC redundancy theory described earlier ([LePage et al., 1993](#)) is consistent with these findings. Earlier sub-clinical damage to some of the OHCs would show up as low-level or absent OAEs, but not necessarily as hearing loss. Further noise exposures damaging further OHCs would then be more likely to lead to hearing loss compared to the ears with more intact OHCs.

Animal studies also provide some clues as to why low-level OAEs could be associated with an increase in the likelihood of future PTS. Chinchilla studies have shown that small amounts of OHC loss have a more significant effect (reduction) on DPOAE amplitude levels than on measures of threshold sensitivity, suggesting that OAEs may also indicate an early onset of cochlear damage in humans ([Davis et al., 2005](#)). These results also suggest that OAEs be considered, within the context of hearing-conservation practices, as a complement to existing hearing-threshold tests in detecting OHC loss resulting from noise exposure. The results indicate that on the basis of threshold information alone, without information about the OAEs, one might underestimate the sensory cell loss. This conclusion is supported by the results of others, which show up to 30% OHC loss in subjects with less than 10 dB of PTS ([Hamernik et al., 1989](#); [Hamernik and Qiu, 2000](#); [Davis et al., 2004](#)). [Bohne et al. \(1987\)](#) also showed that 20%–30% OHC loss in the low frequencies was often not accompanied by corresponding behaviorally measured threshold shifts in the chinchilla. They also explained that a relatively large reduction (12–15 dB) in DPOAEs in the presence of smaller OHC losses at some frequencies may be accounted for not only by the OHC loss but also by morphological changes (e.g., cilia defects or intracellular changes) that can affect the function of cells that are present and for which the cochleogram provides no information.

There were differences between the ears, with no one frequency consistently being a good predictor of the STS status across ears. TEOAEs appeared to be a better predictor of the STS status for the left ear, and DPOAEs appeared to be a better predictor of the STS status for the right ear. Except for TEOAEs at 4 kHz in the left ear, STS risk did not increase greatly until the OAE amplitude moved into the bottom decile.

It is unclear why DPOAEs would be a better predictor of a STS in the right ears and TEOAEs a better predictor of a STS in the left ears. The most likely explanation is that the small number of STS ears contributing to each analysis gives some spurious results. There are other possible contributing factors. The recruits did not get in-depth training on proper insertion of hearing-protection devices; indeed, they sometimes reported that the earplug fell out during the live-fire exercise. [Duvdevany and Furst \(2007\)](#) showed large increases in PTS during a time period when hearing-protection

devices apparently were not worn much. The variability in noise exposure across volunteers could be large compared to the number of Marine recruits that were in this study.

Although we did not keep track of handedness, we would expect approximately 95% of the group to be right handed.¹⁶ Two studies indicated that the left ear is more susceptible to NIHL than is the right ear, irrespective of handedness ([Job et al., 1998](#); [Nageris et al., 2007](#)). In the current study, there was an equal number of STSs in the left ear and the right ear (21 ears for each, including 6 ears with bilateral STS). This indicates that there was considerable noise in the environment (more than just from firing one's own gun), as well as the poor quality of the hearing protection.

Figure 1 indicates that on average the left ear STSs were broader than the right ear STSs, suggesting that the left ear suffered more extensive damage from the impulse-noise exposures than the right ear. The implication is that low-level TEOAEs could be a better predictor of broadband STS and that low-level DPOAEs might be a better predictor of narrowband STS. If this is true, it may be due to higher-order physiological asymmetries (e.g., efferent innervations) that somehow treat tonal stimuli differently from click stimuli depending on which ear the stimuli are presented to (e.g., [Sininger and Cone-Wesson, 2004](#)), but any mechanism is speculative at best. Furthermore, the DPOAE results may be greatly affected by the measurements and data analysis being seen at single widely-spaced frequencies, making it difficult to determine if a low-level DPOAE is just due to the test frequency coinciding with a null in the DPOAE microstructure in what is otherwise a strong DPOAEgram.

Even though we suspect that the apparent differences are due to the relatively small amount of data, the results are suggestive enough that future studies should continue to look at ear differences. If the ear differences seen in this study are also found in future studies, it will be important to parse out whether the differences are due to external factors (e.g., noise exposures), innate factors (e.g., efferent innervation), existing preclinical damage, or methodological idiosyncrasies.

D. Susceptibility to NIHL from impulse noise compared with continuous noise

It is of interest to compare the results of the susceptibility analysis to that in [Lapsley Miller et al. \(2006\)](#), as it is the only other known analysis that considers if OAE amplitude is a predictor of NIHL. Likelihood ratios were used to make this comparison, rather than PPVs, because the PPV is dependent on the prior probability of STS/PTS, which differed across the two studies. The likelihood ratio is a ratio of two probabilities: the probability of a particular test result among patients with a condition to the probability of that particular test result among patients without the condition ([Zhou et al., 2002](#)). In the current context, the likelihood ratio indicates the relative probability that a pre-test OAE amplitude was below a given percentile in the group of ears that subsequently were classified with STS, relative to the same result in the group of ears that did not.

To ensure a fair comparison with [Lapsley Miller et al. \(2006\)](#), ears for the current study were combined, but only

Comparison with Lapsley Miller et al. (2006)

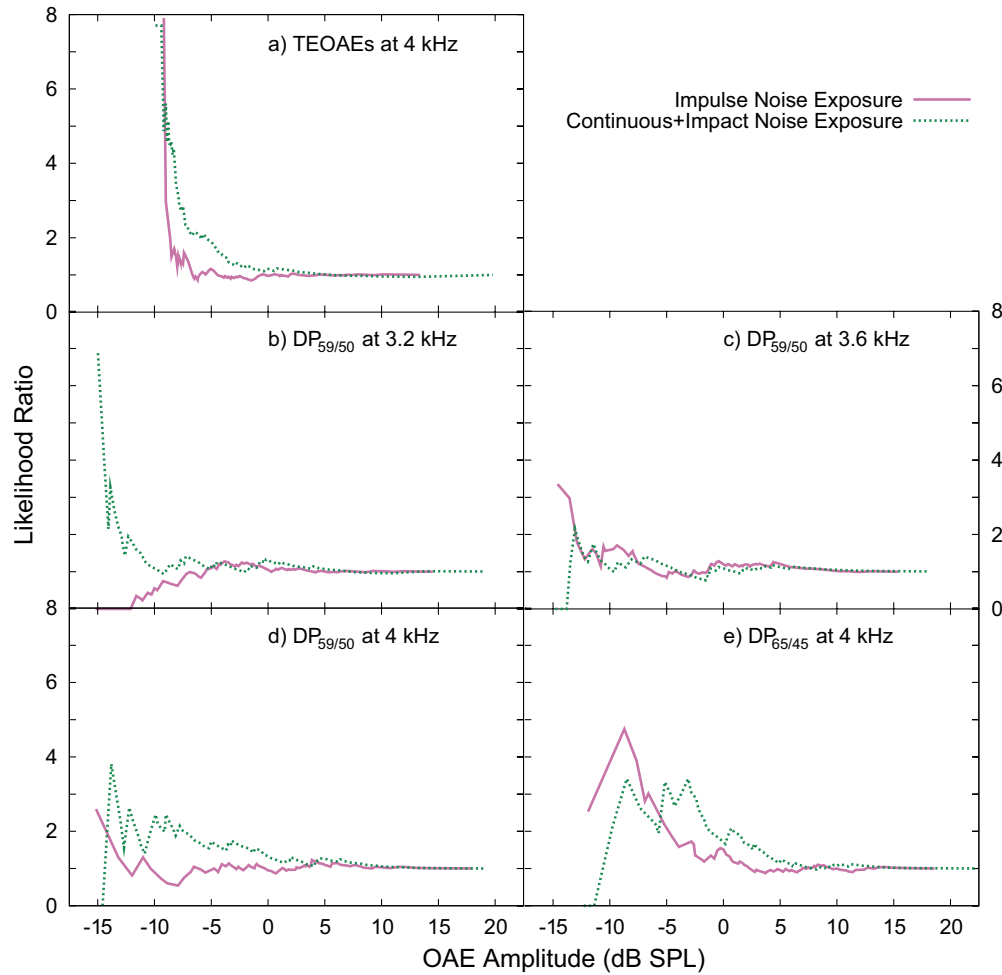


FIG. 9. (Color online) Comparisons of likelihood ratio as a function of OAE amplitude (in dB SPL), indicating susceptibility to noise-induced hearing loss, between the current study (Marine recruits exposed to impulse noise, solid line) and Lapsley Miller *et al.* (2006) (deployed aircraft carrier sailors exposed to continuous noise overlaid with impact noise, dashed line) for the OAE test frequencies where there were no large differences in the amplitude distributions between the ears: (a) TEOAEs at 4 kHz (half-octave band), (b) $DP_{59/50}$ at 3.2 kHz, (c) $DP_{59/50}$ at 3.6 kHz, (d) $DP_{59/50}$ at 4 kHz, and (e) $DP_{65/45}$ at 4 kHz.

for those test frequencies which showed little to no difference in OAE amplitude percentiles between ears.¹⁷ These included TEOAEs at 4 kHz, $DP_{65/45}$ at 4 kHz, and $DP_{59/50}$ at 3.2, 3.6, and 4 kHz. Figure 9 shows likelihood ratio as a function of OAE amplitude. For the current study, likelihood ratios decreased when ears were combined, due to the asymmetry of results between ears. Compared with Lapsley Miller *et al.* (2006), likelihood ratios for the DPOAEs were comparable at 4 kHz. At lower frequencies, the likelihood ratios in the earlier study were higher than for the current study. The biggest difference was for TEOAEs at 4 kHz, with the likelihood ratios in the earlier study showing increased risk for ears with OAE amplitudes below the 50th percentile (approximately 0 dB SPL), whereas for the current study, risk did not increase until about the 5th percentile (approximately -8.5 dB SPL). The maximum likelihood ratio, however, was essentially the same at around 8.

Overall, the general trend across both studies is for low-level OAEs to be predictive of subsequent PTS and/or STS. In both studies, OAEs—particularly TEOAEs—in the 4 kHz region were the best predictors. Larger studies with many more PTS/STS ears are essential to better establish this rela-

tionship. We expect this predictive power to be greater in situations with continuous noise than in situations with impulse noise due to greater variability of the sound power of the sound source reaching the inner ear especially in environments where much gunfire is in the general environment. This supposition is supported by the comparison shown in Fig. 9 where NIHL risk for impulse noise showed up for much lower TEOAE amplitudes, compared with continuous noise. Further, if hearing protectors are not worn (or if they fit poorly) for impulse-noise exposures, we expect the predictive power to diminish even more because there may be sufficient damage over a relatively short amount of exposure time to cause hearing loss irrespective of whether or not there were previously missing OHCs.

When considering both the current and the earlier study, in general, TEOAEs were better predictors than DPOAEs (however, the ear asymmetry shown in the current study indicates that DPOAEs cannot be discounted). There are also a number of mostly practical pros and cons for choosing one OAE type over another. If only a few DPOAE frequencies are tested (which makes the test faster—an important consideration in field studies with humans), it is possible that the

test point will fall into a null of the DPOAE microstructure. To obtain results that are independent of the microstructure, many points per octave need to be measured and averaged (Kemp, 2007), and there are further issues when it comes to combining across frequencies if there are unusable data, particularly when comparing measurements where data may be unusable at different frequencies in different measurements.

Furthermore, the DPOAE measurement is a mix of both reflection-source and distortion-source OAEs (Shera and Guinan, 1999), whereas TEOAEs as measured in humans are essentially reflection source (Withnell *et al.*, 2008). Techniques to separate out the two sources for DPOAEs exist (e.g., Long and Talmadge, 1997; Heitmann *et al.*, 1998; Talmadge *et al.*, 1999; Konrad-Martin *et al.*, 2001; Dhar and Shaffer, 2004; Shaffer and Dhar, 2006; Long *et al.*, 2008), but either are not yet implemented and tested for clinical applications or else have inherent limitations for clinical application (Dhar and Shaffer, 2004). Although in our studies there were more unusable TEOAE data compared with DPOAE data, modern instruments have lower noise floors and faster data collection allowing for more averaging, so we anticipate unusable data to be less of a problem in the future.

E. Concluding remarks

OAEs are predictive of incipient NIHL. It is unknown whether prior noise exposures or innate factors explain why some normal-hearing ears had low-level or absent OAEs. Most recruits indicated that they had prior noise exposures typical of a modern lifestyle, including weapons' fire, amplified music, and machinery noise. Regardless, having a test that indicates ears susceptible to noise-induced hearing loss is a boon for hearing conservation and audiology in general. The current study extends the earlier findings to include impulse noise.

If identifying those individuals and groups most at risk for hearing loss from noise exposure in their near future is possible by detecting the early stages of inner-ear changes, then steps can be taken to prevent or mitigate further damage. While the auditory medial-olivocochlear-bundle reflex (MOCR) may be another way to assess future risk (Maison and Liberman, 2000; Backus and Guinan, 2007), there is at present no test in humans that sufficiently differentiates large and small AERs within the test time available for clinical testing. Furthermore, such a test requires OAEs with reasonable amplitude, thereby precluding the use of such a test in many noise-exposed individuals who do not have strong OAEs. In the future, a very powerful predictive OAE test battery might consist of both OAE level and MOCR strength.

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¹In laboratory studies on humans, only TTSs can be studied, and there is typically a close relationship between changes in OAEs and changes in audiometric thresholds (Marshall and Heller, 1998; Marshall *et al.*, 2001). However, TTSs and PTSs are physiologically different (Saunders *et al.*, 1985; Slepecky, 1986; Nordmann *et al.*, 2000), so the results from TTS experiments cannot be expected to generalize to PTS. Furthermore, laboratory experiments examining PTS in animals may not generalize to humans (see summary in Lapsley Miller *et al.*, 2004, p. 308). Therefore, to understand PTS in humans, there is no substitute for actually measuring PTS in humans. These human PTS experiments invariably have to be conducted in field settings where there is usually neither the time nor facilities to make measurements comparable in quality to those made in the laboratory. Nevertheless, the stated results have been found repeatedly across a range of studies.

²Data from K. S. Wolgemuth from a 1998 study on NIHL from Marine infantry training at Camp Pendleton.

³Data from N. Vause from a 1994 study on NIHL from Army training at Fort Bragg.

⁴Informed consent briefings, conducted by one of the study principal investigators, took place immediately prior to the Marine Corps recruits beginning their medical evaluation on day 2 of basic training. There were approximately 80 recruits in each briefing and Informed Consent forms were passed out prior to beginning the briefing. The recruits were given ample opportunity to ask any questions about the study, and participation was voluntary. The voluntary aspect was made very clear to them given this was a military basic training facility where most activity is mandatory. Approximately 10% of the recruits declined to participate in the study. The volunteers in the control group were also briefed, reviewed the informed consent form, and were asked to participate. The informed consent form was approved under Naval Medical Center, San Diego-approved research protocol No. S-99-085.

⁵It was not possible to control for potential pharmacological influences across subjects, which may have included over-the-counter and prescription medications such as Erythromycin, Motrin, cold medications, and aspirin.

⁶It was not possible to do ANOVA on the control group, because only four volunteers had complete data sets.

⁷As described in Lapsley Miller *et al.* (2006, footnote 6), the SE_{meas} can be used to specify the magnitude of a statistically significant change within an individual (Ghiselli, 1964), and is defined as $SE_{\text{meas}} = \sqrt{\frac{1}{2}(s_1^2 + s_2^2)(1-r)}$ where s_1^2 and s_2^2 are the pre- and post-test variances, and r is the correlation between pre- and post-tests. Because the focus here is on the difference between pre- and post-tests, ΔSE_{meas} is defined as $\sqrt{2}SE_{\text{meas}}$ (Beattie, 2003; Beattie *et al.*, 2003). Multiplying ΔSE_{meas} by an appropriate multiplier then gives the desired confidence interval. Here a multiplier of 2.12 is used, which gives a 98% confidence interval.

⁸13 ears were classified with a STS in just a two- or three-frequency averaged band, and 23 ears were classified with STSs at both individual frequencies and across averaged frequency bands. Six right ears were classified with a STS at only one individual frequency (with no shifts in the contralateral ear). No left ear was classified with a STS at just one frequency.

⁹The other two frequencies in this range (2.8 and 3.6 kHz) were not used as it would increase the false-positive SES rate when detecting SESs for DPOAEs; it was decided that having three frequencies/frequency bands for each OAE type and audiometric threshold would be a fairer balance. Shifts in averaged frequency bands were not considered because too many ears had unusable data at one or more frequencies.

¹⁰SES status could not be determined if (a) the OAE was below the noise floor on the pre-test; (b) the OAE was below the noise floor on the post-test, and the post-test noise floor was high so that the OAE level could not

be estimated; or (c) data loss on the pre-test or post-test.

¹¹In addition, if we had used additional criteria based on averages across frequencies, as we did with STS, the SES rate would be expected to increase, especially as the SES criteria for averaged bands are likely to be smaller thereby allowing smaller wide-band shifts to be detected (Lapsley Miller *et al.*, 2004).

¹²It is not possible to use pre-test audiometric thresholds as predictors here because the volunteers were prescreened for hearing levels. As shown in Fig. 1, pre-test audiometric thresholds were essentially the same for the STS ears compared with the no-STS ears.

¹³SFOAEs are OAEs generated with the same frequency as the evoking tonal stimulus (e.g., Shera and Guinan, 1999).

¹⁴Our implementation of DPOAEs may have also been a factor. We were trying to capitalize on growth functions (testing various stimulus levels at specific frequencies) when, in hindsight, using more frequencies might have been a better bet. By testing with a sparse frequency spacing it is possible that for some ears, some of the test points fell into a null in the DPOAE microstructure (Shaffer *et al.*, 2003). If the DPOAEs had been tested at a sufficient number of frequencies, then we could average them to get the total energy in a frequency band, which would be equivalent in that way to TEOAEs. Of course, it would be a much slower test than the TEOAE test, at least with current instrumentation. In the future, new methods to measure DPOAEs may enable easier comparisons with TEOAEs, and DPOAEs might be less dependent on their implementation (e.g., Long *et al.*, 2008).

¹⁵TEOAEs from lower-level stimuli are more sensitive to cochlear changes due to quinine (Karlsson *et al.*, 1991). Data of ours (to be published) from a study using similar methodology to Marshall and Heller (1998) indicate that TEOAEs evoked with a lower stimulus level show greater sensitivity to noise-induced TTS.

¹⁶For left-handed shooters, an adaptor was used on the rifle range so the recruit would not get hit in the face by a very hot brass shell casing.

¹⁷There were some differences between the two studies: In Lapsley Miller *et al.* (2006), confirmed PTS ears were compared with no-PTS ears, and ears with unconfirmed STS were not included. Ears were combined in analyses, because there were not enough PTS ears (13 left ears and 5 right ears, including 3 bilateral) to analyze ears separately. The noise exposures tended to be continuous noise overlaid with impact noise. For the current study, unconfirmed STS ears were compared with no-STS ears. There were differences between ears in OAE amplitude at many frequencies, so ears were analyzed separately. The noise exposures were impulse noise. OAE amplitude criteria were created from binning into percentile categories, although the results are plotted as a function of OAE amplitude, not percentile. Further, the study was part of a larger study investigating genetic factors of hearing loss, with only a subset of volunteers receiving OAE testing. A blood sample was taken at study enrollment and used to identify those volunteers with the Connexion 26 (35delG) GJB2 polymorphism. Those volunteers with this polymorphism were asked back for OAE testing if they had not already been tested. Thus, the sample had a higher percentage of volunteers with 35delG (13 out of 285; 4.6%) than the general population. Initial analyses did not indicate that the 35delG group was in any way different to the other volunteers, so they were included in all analyses. Only two 35delG volunteers were classified with a STS, which was not sufficient to establish if 35delG was a predictor of STS. Recently, evidence has come to hand showing no relationship between 35delG and NIHL (Van Eyken *et al.*, 2007).

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