Early Indication of Noise-induced Hearing Loss from PMP Use in Adolescents: A Cross-Sectional Analysis

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Abstract

Context: Distortion product otoacoustic emissions (DPOAEs) may indicate preclinical noise-induced hearing loss (NIHL) in adolescents from unsafe personal music player (PMP) use. Aims: The objective, therefore, was to observe preclinical signs of NIHL in 9th grade adolescents with clinically normal hearing by comparing DPOAE signals between different levels of A-weighted equivalent PMP exposure.

Settings and Design: Subjects were recruited from all secondary-level schools located in the city of Regensburg, Germany during two academic years 2009/2010 and 2010/2011. Subjects and Methods: A-weighted equivalent sound pressure levels (SPLs) for a 40-hour work week ($L_{Aeq,40h}$) were estimated from questionnaire responses on output and duration of PMP use of the previous week. Subjects were then categorized into four levels of exposure: <80, 80–85, >85 to <90, and ≥90 A-weighted Decibel [dB(A)]. DPOAE signals were collected by trained audiological staff, applying a standard optimized protocol, at the Department of Otorhinolaryngology of the University Hospital Regensburg. Statistical Analysis Used: Mean DPOAE signals were compared between levels by unpaired t test. Novel linear regression models adjusting for other leisure noise exposures and with outcome variables DPoutcome and 4 kilo Hertz (kHz) DPOAEs estimated effects between levels. Results: A total of 1468 subjects (56% female, mostly aged 15 or 16 years) were available for analysis. Comparison of DPOAE means by PMP exposure typically showed no greater than 1 dB difference between groups. In fact, comparisons between ≥90 dB(A) and <80 dB(A) presented the least differences in magnitude. Both DPoutcome and 4kHz linear regression models presented a weak association with the 4-level PMP exposure variable. An expected dose-response to PMP exposure was not observed in any analyses.

Conclusions: DPOAE signal strength alone cannot indicate preclinical NIHL in adolescents.

Keywords: Adolescent, distortion product otoacoustic emissions, noise-induced hearing loss, ohrkan study, personal music players

INTRODUCTION

Both the WHO and European Commission’s Scientific Committee on Emerging and Newly Identified Health Risks (SCENIHR) have expressed concern over the risk of noise-induced hearing loss (NIHL) in adolescents from unsafe exposure to personal music player (PMP) noise.[1,2] A recent press release by the WHO emphasized that “1.1 billion teenagers and young adults are at risk of hearing loss (HL) due to the unsafe use of personal audio devices....”[3] Despite such warnings and studies showing output levels of popular PMPs can exceed 85 A-weighted Decibel [dB(A)][4-7] (the upper occupational limit of Directive/2003/10/EC[8]), no official safety standards regulating the appropriate use of PMPs exist anywhere. Risk of NIHL from unsafe PMP use is, therefore, a legitimate public health concern that warrants attention.

In recent years, there have been developments regarding the biology and clinical application of otoacoustic emissions (OAEs). Studies conducted in occupational settings suggest that distortion product otoacoustic emissions (DPOAEs) may predict the development of NIHL.[9,10] Additionally, biological studies have shown that NIHL affects the order and integrity of outer hair cells (OHCs) within the cochlea,[11,12] and that these are the likely source of DPOAEs.[13] In light of these findings,

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DPOAE signal strength may be a useful indicator of preclinical NIHL in at risk individuals.

Studies comparing DPOAE signal strength between PMP exposure levels are inconclusive largely due to methodological differences particularly with regard to exposure assessment (see Discussion). These studies were also not exclusive to adolescents, a commonly perceived at risk group. In the present study, we analyzed cross-sectional data from 9th grade adolescents with clinically normal hearing to explore whether PMP exposures above established occupational limits present weaker DPOAE signal strength which could indicate preclinical NIHL.

**Subjects and Methods**

Analysis data were collected during the baseline phase of the Ohrkan cohort study, initiated by the Bavarian State Office for Health and Food Safety and funded by the Bavarian State Ministry of Health and Care. More information on the design of the Ohrkan study and the analysis of baseline audiometric data can be found elsewhere.[14,15] Ohrkan was approved by the Ethics Committee of the University of Regensburg. Recruitment of subjects and baseline data collection took place from October 2009 to July 2011.

**Recruitment of subjects**

Adolescent subjects were recruited in Regensburg, a city of approximately 135,000 residents in the state of Bavaria, Germany. The minimum eligibility requirement was that subjects be in the 9th grade during recruitment at any secondary-level school in the city of Regensburg. Information sheets and questionnaires were distributed at schools followed by an information session a week later. Subjects were asked to review the materials at home with their parents. Signed informed consent forms were obtained to only use DPOAE data from subjects with an SNR greater than 20 dB. To assess reliability of the data, the signal-to-noise ratio (SNR) was calculated for each recording by subtracting the noise amplitude (dB) from the signal amplitude (dB) due to these DPOAE amplitudes and 18 background noise level amplitudes measured.

**Collection of questionnaire data and related analysis variables**

Subjects completed a standardized questionnaire on socio-demographic factors, noise exposures, self-reported hearing ability, and tinnitus. Another standardized questionnaire was given to parents (or legal guardians) for data on socio-demographic factors and medical history of the subject.

Before the collection of audiological data, students were required to complete a short standardized survey asking about noise exposure within the last 24 h as well as current conditions that could affect hearing ability. To maximize response, subjects received a gift certificate to a local cinema and prizes with an overall value of 3000 were raffled.

Variables on sex, age, school type, school ownership, country of birth, migration background, parental education, marital status, and single parenthood used in our analysis, were previously created based on responses from the student and parent questionnaires. See Twardella et al.[15] for description of variables. These variables were used in demographic characterization and adjusted for in linear regression analyses.

PMP exposure was previously calculated by Twardella et al.[16] using subject’s responses on duration and output levels from the previous week. The 40-hour A-weighted equivalent sound pressure level (SPL) exposure was calculated applying the following formula:

\[ L_{\text{Aeq,40h}} = L_{\text{Aeq,Tc}} + 10 \log \left( \frac{T_e}{T_0} \right) \]

where \( L_{\text{Aeq,Tc}} \) represents the estimated SPL, \( T_e \) the reported exposure time in hours per week and \( T_0 \) the reference duration of 40 h.[16,17] Acknowledging that the lower (80 dB(A)) and upper (85 dB(A)) occupational limits are necessary to distinguish NIHL between subjects, A-weighted equivalent SPLs for a 40-hour work week (\( L_{\text{Aeq,40h}} \)) values were categorized into four levels ((1) <80 dB(A)), (2) 80–85 dB (A), (3) >85 to <90 dB(A), and (4) ≥90 dB(A)) of PMP exposure to create a new main exposure variable.

Data on the 40-hour A-weighted equivalent exposure from other leisure noise exposures such as from loudspeakers, playing computer games with headphones, playing in a band, attending a discotheque, etc. were also available, but based on responses regarding yearly exposure instead of weekly.

**Collection of audiological data and related variables**

All audiological tests were performed at Department of Otorhinolaryngology of the University Hospital Regensburg by resident clinical staff applying routine standardized protocols. Subjects were primarily responsible for attending the testing session.

The collection of tympanometry and audiometry data has been previously described by Twardella et al.[15]

DPOAE signal amplitudes (dB) were recorded at the at the \( 2F_2–F_1 \) frequency using ILO v292 software in a double walled, sound-attenuated room to minimize ambient noise level. A fitted probe was inserted into the ear and clipped to the subjects clothing to prevent noise from friction with clothing. The \( 2F_2–F_1 \) frequency was chosen because it is accepted as the largest measurable DPOAE signal in human ears and the most reliable.[18,19] To achieve this, the \( F_2/F_1 \) ratio was fixed at 1.22 and the \( L_{\text{L}}/L_{\text{L2}} \) to 65/55 dB SPL for all recordings. DPOAEs were measured for 9 \( F_2 \) frequencies of 1, 1.26, 1.587, 2, 2.52, 3.175, 4, 5.04, and 6.35 kilo Hertz (kHz) for each of the subject’s ears. Ideally each subject should have a total of 18 DPOAE signal amplitudes and 18 background noise level amplitudes measured.

To assess reliability of the data, the signal-to-noise ratio (SNR) was calculated for each recording by subtracting the noise amplitude (dB) from the signal amplitude (dB) due to these being logarithmic values.

A new variable termed \( DP_{\text{outcome}} \) was generated to be a dependent variable for linear regression analyses. The variable was defined in accordance to the definition of an audiometric notch (AN) which is characterized by worse hearing levels in the high frequency range in comparison to the low frequency range.[20] For this, it was first necessary to only use DPOAE data from subjects with an SNR > 6 in all
test conditions. To compute, DPOAEs were grouped as *high frequency* if measured from 4 to 6 kHz and *low frequency* if from 1.587 to 2 kHz. Means were estimated for each group and the mean of the *high frequency* range was subtracted from the *low frequency* range to obtain the mean difference for each ear side. Of the two ear mean differences, the lower value was taken as the final value of DPoutcome, assuming it indicated the more impaired ear of the two.

DPOAEs at 4 kHz for the left and right ear each were also used as dependent variables for regression analyses. Since the 4 kHz region has previously been observed as the site most impaired by NIHL from occupational noise,[21] we thought it could serve as a valid indicator of NIHL. As a control analysis to establish that observed effects were indeed specific to the 4 kHz region, the same regression analyses were also performed with 1.587 kHz.

**Inclusion/exclusion criteria for analyses**

Subjects were included in the analysis based on the following criteria:

1. Normal hearing based on tympanometry and audiometry results (no AN, no low- or high frequency HL).[17,20,22]
2. No underlying hearing pathologies based on questionnaire responses on hearing aid use and previous physician diagnosed tinnitus (PDT).
3. Complete DPOAE measurement data (18 signal, 18 noise).
4. Complete PMP exposure data ($L_{Aeq,40h}$).
5. Reliable DPOAE measurement data based on SNR > 6.

If a subject had an SNR < 6 for some but not for all 18 DPOAE tests, then the data (signal and noise) for that ear/ frequency specific test were labeled as *missing*.

**Statistical methods**

Descriptive characterization of subjects was based on demographic background and a variety of leisure noise exposures. Subjects were further stratified by whether their equivalent PMP exposure was above/at or below 80 dB(A). Chi-squared test were performed to find an association between a given variable and PMP exposure.

DPOAE means were calculated by frequency and ear side for each PMP exposure group. The significance of differences between means was tested by unpaired *t* test. A difference was considered significant if $P < 0.05$.

As a peripheral analysis to control for validity, the frequency- and ear specific DPOAE means of subjects with an AN were compared to our final sample by unpaired *t* test and considered significant if $P < 0.05$. A subject failed audiometric testing if they presented a notch in at least one ear that satisfied the criteria posed by Niskar *et al.*[20] and Twardella *et al.*[15]

Overall seven multiple linear regression models were applied in both outcome analyses to observe changes in effect estimates after adjusting for covariates. Selection of variables for inclusion was based mainly on Chi-square *P*-values from the sample characterization. If a given variable had a *P*-value of 0.1 or lower it was included in the regression analysis. Pearson correlation coefficients (*r*) were used to check for correlation between potential covariates. If *r* was greater than 0.25, the two variables were not included in the same model together. Additionally, the variance inflation factor (VIF) was consulted to exclude variables from a certain model; if more than 4 then the variable was excluded. Covariates included in all final models had a VIF around 1. Owing to correlation between some demographic covariates, separate models, each including a unique group of demographic covariates, were applied.

As this analysis was exploratory in nature, no Bonferroni correction of estimates was performed.

All manipulations were performed in Statistical Analysis System (SAS) v9.2.

**RESULTS**

**Subject selection for analysis**

From 3846 eligible students, 2148 (55.9%) agreed to participate in the *Ohrkan* study and 1932 (50.2%) participated in audiological testing [Figure 1]. After applying inclusion/ exclusion criteria a total of 680 (31.7%) of the original 2148...
were excluded from analysis, resulting in 1468 (68.3%) subjects available for analysis.

**Description of final sample**

Characterization by demographic characteristics revealed that 56% of subjects were female and 45% were 15 years of age [Table 1]. The most prevalent school type was university preparatory school (UP, 50%). Largely represented categories were attending public school (70.3%), German birth (92.4%), no migration background (77.2%), having parents with a high education (57.0%), having parents in a married or registered partnership (77.5%), and not having single parents (81.1%). Demographics found to be significantly associated with a PMP exposure above or below the lower limit of 80 dB(A) by Chi-square were age, school type, country of birth, migration background, parental education, parent marital status, and whether the parent had a single parenthood ($P < 0.05$).

### Table 1: Characterization of study population by demographics

| Demographic                              | Final sample ($n = 1468$) | $<80$ dB(A) PMP $L_{Aeq,40h}$ ($n = 1098$) | $\geq 80$ dB(A) PMP $L_{Aeq,40h}$ ($n = 370$) | Chi-square | $P$-value |
|------------------------------------------|---------------------------|---------------------------------------------|---------------------------------------------|------------|------------|
| **Sex**                                  |                           |                                             |                                             |            |            |
| Female                                   | 821 (55.9)                | 627 (57.1)                                 | 194 (52.4)                                 | 0.12       |            |
| Male                                     | 647 (44.1)                | 471 (42.9)                                 | 176 (47.6)                                 |            |            |
| **Age (years)**                          |                           |                                             |                                             |            |            |
| 13 or 14                                 | 183 (12.6)                | 132 (12.1)                                 | 51 (14.0)                                  | 0.001      |            |
| 15                                       | 652 (44.8)                | 516 (47.3)                                 | 136 (37.3)                                 |            |            |
| 16                                       | 493 (33.8)                | 363 (33.2)                                 | 130 (35.6)                                 |            |            |
| 17–19                                    | 129 (8.9)                 | 81 (7.4)                                   | 48 (13.2)                                  |            |            |
| Missing                                  | 11 (0.8)                  | 6 (0.6)                                    | 5 (1.4)                                    |            |            |
| **School type**                          |                           |                                             |                                             |            |            |
| Special learning needs school (Förderschule) (SLN) | 40 (2.7)                | 24 (2.2)                                   | 16 (4.3)                                   | <0.0001    |            |
| General/vocational schools for non-university bound students (Haupt-/Mittelschule) (GV) | 335 (22.8)                | 218 (19.9)                                 | 117 (31.6)                                 |            |            |
| Professional/business schools (real-/Wirtschaftschule) (PB) | 360 (24.5)                | 256 (23.2)                                 | 104 (28.1)                                 |            |            |
| University preparatory school (gymnasium) (UP) | 733 (49.9)                | 600 (54.6)                                 | 133 (36.0)                                 |            |            |
| **School ownership**                     |                           |                                             |                                             |            |            |
| Public                                   | 1032 (70.3)               | 771 (70.2)                                 | 261 (70.5)                                 | 0.91       |            |
| Private                                  | 436 (29.7)                | 327 (29.8)                                 | 109 (29.5)                                 |            |            |
| **Country of birth**                     |                           |                                             |                                             |            |            |
| Germany                                  | 1352 (92.4)               | 1020 (93.3)                                | 332 (89.7)                                 | 0.02       |            |
| Abroad                                   | 111 (7.6)                 | 73 (6.7)                                   | 38 (10.3)                                  |            |            |
| Missing                                  | 5 (0.3)                   | 5 (0.3)                                    | 0                                          |            |            |
| **Migration background**                 |                           |                                             |                                             |            |            |
| None                                     | 1098 (77.2)               | 842 (79.1)                                 | 256 (71.5)                                 | 0.01       |            |
| Possible                                 | 124 (8.7)                 | 87 (8.2)                                   | 37 (10.3)                                  |            |            |
| Yes                                      | 200 (14.1)                | 135 (12.7)                                 | 65 (18.2)                                  |            |            |
| Missing                                  | 46 (3.1)                  | 34 (3.1)                                   | 12 (3.2)                                   |            |            |
| **Parental education**                   |                           |                                             |                                             |            |            |
| Low                                      | 196 (13.7)                | 126 (11.8)                                 | 70 (19.3)                                  | <0.0001    |            |
| Medium                                   | 420 (29.3)                | 286 (26.7)                                 | 134 (36.9)                                 |            |            |
| High                                     | 817 (57.0)                | 658 (61.5)                                 | 159 (43.8)                                 |            |            |
| Missing                                  | 35 (2.4)                  | 28 (2.6)                                   | 7 (1.9)                                    |            |            |
| **Marital status**                       |                           |                                             |                                             |            |            |
| Single                                   | 57 (3.9)                  | 35 (3.2)                                   | 22 (6.0)                                   | 0.0003     |            |
| Married/registered partnership           | 1127 (77.5)               | 871 (80.0)                                 | 256 (70.1)                                 |            |            |
| Divorced                                 | 239 (16.4)                | 158 (14.5)                                 | 81 (22.2)                                  |            |            |
| Widowed                                  | 31 (2.1)                  | 25 (2.3)                                   | 6 (1.6)                                    |            |            |
| Missing                                  | 14 (1.0)                  | 9 (0.8)                                    | 5 (1.4)                                    |            |            |
| **Single parenthood**                    |                           |                                             |                                             |            |            |
| No                                       | 1181 (81.1)               | 903 (82.8)                                 | 278 (76.0)                                 | 0.004      |            |
| Yes                                      | 275 (18.9)                | 187 (17.2)                                 | 88 (24.0)                                  |            |            |
| Missing                                  | 12 (0.8)                  | 8 (0.7)                                    | 4 (1.1)                                    |            |            |
Characterization by other leisure noise exposures [Supplementary Table S1] revealed that most subjects typically had an exposure of <80 dB(A) for other leisure noise activities besides PMP use. Exposures significantly associated with a PMP exposure by Chi-square were loudspeakers, listening to a sound system with headphones, playing computer games with headphones, attending a popular music concert, a discotheque, a sports stadium, and playing indoor ball sports ($P < 0.05$).

**Comparison of DPOAE data between PMP exposure levels and audiometric results**

Categorizing by PMP exposure showed that 1098 (74.8%) subjects had <80 dB(A), 128 (8.72%) 80–85 dB(A), 72 (4.9%) >85 to <90 dB(A), and 170 (11.6%) ≥90 dB(A) [Supplementary Table S2]. Although there were some significant differences found by unpaired $t$ test, overall the DPOAE means of the higher exposure groups showed little difference to that of the <80 dB(A) [Figure 2]. Differences in means were typically around 1 dB in size [Supplementary Table S2]. Counterintuitively, the ≥90 dB(A) exposure had the closest values to the <80 dB(A) group [Supplementary Table S2, “bottom”].

The analysis to control for validity, comparing subjects in the final sample ($n = 1468$) with subjects who presented an AN, ($n = 35$), showed that AN subjects with lower mean DPOAE signals for all frequencies in both ear sides, though differences were usually only a few decibels lower [Figure 3 and Supplementary Table S2]. Differences were, however, a few decibels larger than those seen between PMP levels in Figure 2 [Supplementary Table S2]. Moreover, unlike PMP comparisons, significant differences by unpaired $t$ test were found at almost all frequencies except 1 and 4 kHz in the left ear, and at 1.587, 2, and 2.52 kHz for the right ear ($P < 0.05$).

**Linear regression with DPOAE outcomes**

A total of 840 subjects (57.2%) had reliable data (SNR > 6) for all DPOAEs collected, and therefore were isolated for linear regression with $D_{outcome}$. Of these, 640 (76.2%) had a PMP exposure <80 dB(A), 66 (7.9%) 80–85 dB(A), 35 (4.2%) >85 to <90 dB(A), and 99 (11.8%) ≥90 dB(A). The effect on $D_{outcome}$ estimated for each of the upper PMP exposure groups, were typically between 0 and 1 [Table 2]. Moreover, the 95% confidence intervals typically included 0. Only an exposure ≥90 dB(A) presented significant estimates with $D_{outcome}$ in Model 1 and after adjusting for sex in Model 2. The 80–85 dB(A) group had a positive effect on $D_{outcome}$ in all models, though none were significant. The >85 to <90 dB(A) group, which was also smallest in size, had a similar effect for most models as the ≥90 dB(A) group, but estimates were not significant and confidence intervals were wider in this group than the others. Overall a clear dose response was not observed between PMP exposure and $D_{outcome}$.

*Figure 2:* Mean DPOAE ($2F_1-F_2$) amplitudes (DP) and noise levels (NL) at each frequency between [<80 dB(A)] and [(a and b) 80–85 dB(A), (c and d) >85 to <90 dB(A), and (e and f) ≥90 dB(A)] for left and right ears. Significant differences in means from unpaired $t$ test are given by * for $P < 0.05$ and ** for $P < 0.01$.
Table 2: Linear regression with DPOAE dependent variables

| DPoutcome (n = 840) | 80–85 (n = 66) | >85 to <90 (n = 35) | ≥90 (n = 99) |
|---------------------|----------------|---------------------|-------------|
| β | 95% CI | β | 95% CI | β | 95% CI |
| Model 1* | 0.48 | −0.75, 1.71 | −1.14 | −2.79, 0.51 | −1.04 | −2.07, −0.01* |
| Model 2b | 0.50 | −0.73, 1.73 | −1.09 | −2.75, 0.57 | −1.04 | −2.06, −0.01* |
| Model 3c | 0.68 | −0.56, 1.93 | −0.80 | −2.49, 0.90 | −0.93 | −2.01, 0.15 |
| Model 4d | 0.42 | −0.86, 1.70 | −1.01 | −2.69, 0.67 | −0.72 | −1.82, 0.38 |
| Model 5e | 0.52 | −0.72, 1.75 | −0.80 | −2.48, 0.88 | −0.85 | −1.92, 0.21 |
| Model 6f | 0.68 | −0.57, 1.93 | −0.51 | −2.22, 1.20 | −0.79 | −1.89, 0.30 |
| Model 7g | 0.46 | −0.82, 1.74 | −0.70 | −2.41, 1.00 | −0.50 | −1.63, 0.63 |

4 kHz DPOAE (n = 1468)

| 80–85 (n = 128) | >85 to <90 (n = 72) | ≥90 (n = 170) |
|-----------------|---------------------|-------------|
| β | 95% CI | β | 95% CI | β | 95% CI |
| Model 1d | −1.27 | −2.34, −0.20* | −1.20 | −2.58, 0.19 | −1.04 | −2.03, −0.05* |
| Model 2e | −1.26 | −2.33, −0.19* | −1.09 | −2.48, 0.29 | −1.03 | −2.01, −0.04* |
| Model 3f | −1.15 | −2.25, −0.06* | −0.72 | −2.14, 0.70 | −0.88 | −1.79, 0.12 |
| Model 4g | −1.08 | −2.19, 0.03 | −0.82 | −2.23, 0.59 | −0.93 | −1.94, 0.09 |
| Model 5h | −1.22 | −2.31, −0.14* | −1.07 | −2.47, 0.33 | −0.97 | −1.97, 0.03 |
| Model 6i | −1.14 | −2.24, −0.03* | −0.68 | −2.12, 0.75 | −0.83 | −1.84, 0.19 |
| Model 7j | −1.09 | −2.22, 0.03 | −0.80 | −2.23, 0.63 | −0.90 | −1.93, 0.13 |

*P < 0.05. aUnivariate model. Reference group for all models estimates is <80 dB(A) PMP exposure. bAdjusted for sex of subjects. cAdjusted for sex, age, country of birth, level of parents’ education, and relationship status of parents. dAdjusted for sex, migration background, school type, parents’ education, and single parenthood. eAdjusted for exposure from loudspeakers, computer games with headphones, playing a musical instrument, attending a rock, pop, or jazz concert, attending a discotheque, visiting a sports arena, and performing indoor ball sports. fAdjusted for sex, age, country of birth, level of parents’ education, relationship status of parents, exposure from loudspeakers, computer games with headphones, playing a musical instrument, attending a rock, pop, or jazz concert, visiting a sports arena, and performing indoor ball sports. gAdjusted for sex, migration background, school type, parents’ education, single parenthood, loudspeakers, computer games with headphones, playing a musical instrument, attending a rock, pop, or jazz concert, attending a discotheque, visiting a sports arena, and performing indoor ball sports.

Figure 3: Mean DPOAE (2F1−F2) amplitudes (DP) and noise levels (NL) of those in final sample and those who presented an audiometric notch (AN) by frequency for (a) left and (b) right ears. Significant differences in means from unpaired t tests are given by * for P < 0.05 and ** for P < 0.01.

Applying the same models with right and left 4 kHz DPOAE signals as outcomes generated negative effect estimates in all models [Table 2]. Unlike DPoutcome, the lowest estimates were observed with a PMP exposure ≥90 dB(A), and the largest with an 80–85 dB(A) exposure for both ears. Again, no dose response was observed. Nearly all effect estimates for the left ear with an exposure of 80–85 dB(A) were significant, except Models 4 and 7 which both adjusted for the same set of demographics. Models 1 and 2 were also significant in the right ear with an exposure of 80–85 dB(A), and also with >85 to <90 dB(A). Most estimates though were near 0 or 1 in magnitude, and the respective confidence intervals typically included 0. A control regression with 1.587 kHz DPOAE for the left and right ear each as the outcome variable did not reveal consistently weaker estimates, which otherwise would be the case if the 4 kHz had indeed been affected (data not shown).
DISCUSSION

The objective was to explore whether DPOAE signals alone can indicate preclinical NIHL from unsafe PMP use in adolescents with otherwise normal hearing. Our results suggest that the magnitude of DPOAE signals alone does not indicate large differences in hearing quality between occupationally higher and lower PMP exposure levels, which were previously not detected by pure tone audiometry (PTA). Results from unpaired t tests showed little difference in frequency- and ear specific DPOAE means between exposure groups. Although some significant differences in means between groups were found, these were not consistent by ear side or frequency, as would be expected with permanent acoustic trauma. There was also a high overlap in the standard deviations for all mean comparisons between groups, suggesting that means are within the same range of magnitude. To ensure our mean comparisons were valid, we compared the DPOAE means of AN subjects with that of our final sample. This showed that DPOAEs are somewhat sensitive to differences in hearing quality though differences were at most a little dB in volume. Differences were typically smaller at higher frequencies and vice versa, but were inconsistent with NIHL pathogenesis. Linear regression modeling with outcome variables, DPoutcome and the left- and right 4 kHz DPOAE signals, presented weak effect estimates between PMP exposure and each outcome. A dose response to PMP exposure level, which would be needed for screening of preclinical NIHL, was not observed in any analyses. Results indicate that although there were some differences in DPOAEs between exposure groups, these were not large and consistent to demonstrate that DPOAE signal strength alone could be a screening tool for preclinical NIHL in a sample of adolescents with clinically normal hearing. A reason could be that alterations in the cochlea at this early stage are too minuscule to affect a large and consistent change in DPOAE signal strength. Alternatively, subjects may have no any OHC damage from listening because they have not had such chronic exposure as is common in occupational settings.

A review of previous studies by Kumar et al.,[4] Lee et al.,[6] Marron et al.,[7] Sulaiman et al.,[23] Peng et al.,[24] Torre et al.,[25] and Santaolalla Montoya et al.[26] comparing DPOAE signal strength between PMP exposure groups provided inconclusive results. Variability in the exposure assessment between studies, which included subjects from the United States, Spain, China, Malaysia, India, and Singapore, may have been an underlying reason. Ideally PMP exposure should reflect both the output and duration of use on the subject’s own preferred music player while at leisure. The only studies reviewed that actually fulfilled this were Kumar et al.[4] and Marron et al.,[7] which represent two of the seven similar studies found. Both studies measured the output levels of each subject’s PMP while listening to one of their preferred songs, and determined the listening duration per day by questionnaire in order to calculate the A-weighted equivalent SPL for an 8h day. Groups were then categorized as <80 dB(A), >80 dB(A), and non-users. Interestingly both studies also reported no significant differences between the DPOAE means of each group. However, Kumar et al. was the only study of the two that included subjects in the age range of teens to early twenties. Whereas Marron et al. included subjects from the ages of 18–84 years who may have had damage from other sources besides PMPs.

Comparatively the remaining studies lacked incorporation of both output and duration in their exposure assessment. Many, like in the case of Peng et al.,[24] Torre et al.,[25] and Santaolalla Montoya et al.[26] only accounted for duration and not output level. This might have been in order to focus on long-term or chronic exposure, which is a known preclude to NIHL. The possibility of impulse noise exposure which is also known to cause NIHL in subjects should however not be excluded. Lee et al.[6] also calculated A-weighted SPLs but were not measured using the subject’s own player but a provided Apple iPod Nano. Sulaiman et al.[23] also calculated the 8-hour A-weighted equivalent SPLs for each subjects; however, these values were not used in DPOAE analysis but only in the analysis of audometric data. The most general exposure assessment of those found was by Peng et al.[24] in which the comparison of DPOAE means was between “users” and “non-users,” which was only assessed by asking subjects if they use a PMP. Audiological testing was for the most part similar between studies. The overall procedure followed in the studies typically consisted of pre-examination by otoscopy and tympanometry to confirm normal pathology, followed by PTA to assess the subject’s hearing threshold, and lastly culminated with the recording of OAEs, which in some studies involved both DPOAEs and Transient-Evoked Otoacoustic Emission (TEOAEs). All studies confirmed external and middle ear function by performing otoscopic examination and tympanometry beforehand on subjects. With the exception of Sulaiman et al., and Marron et al., most also included in their analysis subjects who passed audiometric examination based on a threshold level that was usually lower than 15, 20, or 25 dB HL at all frequencies tested. Lee et al. was the only study that made no mention of performing audiometric examination. We specifically excluded subjects with abnormal audiometry results as a way to assess whether DPOAE signals could detect permanent hearing damage unnoticed by PTA (the current gold standard). Therefore, results from Sulaiman et al., Marron et al., and Lee et al., are not directly comparable to our study, which had a novel and specific objective of observing preclinical NIHL in adolescent subjects. Though it is difficult to confirm, this may have also produced other methodological differences found between this and the other studies.

The recording of DPOAE signals was also more or less similar between studies. All studies measured DPOAEs at the 2F2–F1 frequency. L1/L2 stimulus levels of 65/55 dB SPL were applied in four of the seven studies. In studies by Montoya et al., Peng et al., and Torre et al., it is unclear why alternative stimuli (70/40, 70/65, 55/40 dB SPL) were
chosen when 65/55 dB SPL is commonly known, in combination with the other parameters, to produce the most robust DPOAE signal at the $2F_2-F_1$ frequency. The $F_2$ frequencies at which DPOAEs were recorded varied between studies which could have also affected comparability.

Other factors which may have compromised comparability of results are whether testing was performed in a sound-attenuated room in order to prevent interference of the DPOAE signal from ambient noise, the recording software used, whether trained staff performed testing, if subjects were asked to refrain from listening to PMPs or other sources of loud noise the day before testing, and whether the reliability of DPOAEs was assessed by SNR value. Except for Lee et al., all studies performed testing in a sound-attenuated room. Each study applied a different software for recording DPOAEs, though it is unknown how this could have influenced results. Surprisingly, no study mentioned whether trained staff performed audiological testing. A lack of expertise in DPOAE recording may explain why some studies opted for non-optimal stimuli during testing. Kumar et al., Marron et al., and Torre et al. did not mention asking subjects to refrain from listening to PMPs or other loud noise the day before testing took place. This may have compromised the reliability of DPOAE signals. SNR was also not mentioned in most studies, except Sulaiman et al. which used a cutoff of SNR > 0 to include subjects. It should be noted that in the case of DPOAEs, the SNR is the ratio between the DPOAE signal and the background noise level measured. By neglecting the SNR, some studies may have inadvertently included DPOAE signals which were not distinguishable from low-level background noise present during testing.

We took many precautions to ensure the quality of our study’s results. To include both the output and duration of PMP usage in our exposure assessment, as well as to permit comparability with occupational standards, the 40-hour A-weighted equivalent SPLs were calculated. Although output levels were not directly measured, questionnaire reported output levels were externally validated by asking subjects not involved in the study to confirm the output levels from their own PMPs. Data on several demographics and other leisure noise exposures were also collected by questionnaire, which allowed for the characterization of our sample population and adjustment in regression analysis. During the collection of all audiological data, trained technical staff performed all tests in a clinical setting. To assure quality of results during analysis, DPOAE measurements with an SNR < 6 dB were excluded, which was more stringent than commonly applied. We also included novel multiple regression models in our analysis that included DPoutcome and the 4 kHz DPOAE signal as outcome variables, a 4-level variable of PMP exposure, and adjusted for demographics and other leisure noise variables.

When interpreting the results of this study, some limitations should also be considered. Misclassification of exposure level due to several factors could explain why a dose response was not observed in any analyses. It may also explain why DPOAE means for the highest exposure group (≥90 dB (A)) were closest in magnitude to those of the lowest group (<80 dB(A)). A possible source of exposure misclassification could be due to output levels of subjects’ PMPs not being directly measured but assessed only by questionnaire, which may have produced recall bias in some cases. We attempted to mitigate this by externally validating our technique. However, errors in recalling output levels were still possible. Subjects with poorer memory or a lower educational background could have had more difficulty recalling their volume setting and duration of use. Concerning assessment of duration, subjects were asked about their exposure for the previous week only, and not for an extended period of time, to minimize recall bias. This, however, may not represent the typical weekly exposure over the course of a longer period of time (e.g., a year). We can expect though that what the subjects provided was their typical exposure, since any atypical variations in use were unlikely to be mentioned. Exposure misclassification could also have come from a Hawthorne effect, whereby subjects altered their responses as a result of their awareness of being investigated. Within our response pool, it is possible that subjects with higher exposures altered their questionnaire responses to be categorized as lower. This could especially be true when we consider that subjects were pre-informed about the hazards of excessive loud noise during the information session held at schools. Instrument bias was unlikely to affect our results since standard procedures and calibration were performed throughout testing by trained staff. It should also be mentioned that this study was meant as an exploratory analysis and that for this reason we did not apply a Bonferroni or other correction of multiple testing. The exploratory approach of our analyses may have also led to overadjustment of variables in regression modeling.

More studies with stringency in data collection, exposure assessment, and analysis, as well as larger sample size need to be duplicated in other regional and demographic contexts to provide conclusive results. Since subjects in all such previous studies tended to be young adults, more studies analyzing DPOAEs of adolescent subjects are also needed. Future studies should also provide A-weighted equivalent SPLs for PMP exposure, apply an optimal DPOAE protocol such as the one mentioned here, and remove DPOAE data with an SNR < 6 in order to ensure the reliability and comparability of their results. In the case of untrained study personnel looking to record DPOAEs, it would be best to consult with a trained clinical audiologist to monitor and inform all testing procedures. Our results indicate that DPOAE signal strength cannot indicate preclinical NIHL from unsafe PMP use in adolescents with normal hearing. At this stage it is difficult to predict whether subjects with PMP exposures higher than occupational standards will develop NIHL in the future. Subjects may still be too young for DPOAE signal...
strength to reflect minuscule damage from unsafe PMP use. Alternatively, there may be no permanent damage present due to the young age of subjects. This could explain why a dose response to PMP exposure was not observed, but it does not completely explain why DPOAE means of the ≥90 dB(A) group were closer in magnitude to the <80 dB(A) group, than the 80–85 dB(A) and >85 to <90 dB(A) groups. The latter could instead be explained by exposure misclassification. Early indication of preclinical NIHL would greatly aid the prevention of NIHL among adolescents and young adults, as well as other high risk groups. Other methods such as an established DPOAE threshold may be more helpful in identifying those at risk than DPOAE signal strength alone.

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Conflicts of interest
There are no conflicts of interest.

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## I. Supplementary

### Table S1 - Characterization of Study Population by Leisure Noise Exposure

| Leisure Noise                | Final Sample | <80dB(A)     | ≥80 dB(A)    | Chi-square | P-value |
|------------------------------|--------------|--------------|--------------|------------|---------|
|                              | (n=1468)     | PMP $L_{A_{eq},40h}$ | PMP $L_{A_{eq},40h}$ |            |         |
|                              | N (column %) | (n=1098)     | (n=370)      |            |         |
|                              | N (column %) | N (column %) |             |            |         |
| **Phone Type**               |              |              |              |            |         |
| Earbuds                      |              |              |              |            |         |
|                              | 1124 (92.4)  | 790 (92.8)   | 334 (91.3)   | 0.34       |         |
| Headphones                   |              |              |              |            |         |
|                              | 93 (7.6)     | 61 (7.2)     | 32 (8.7)     |            |         |
| Missing                      |              |              |              |            |         |
|                              | 251 (17.1)   | 247 (22.5)   | 4 (1.1)      |            |         |
| **Moped**                    |              |              |              |            |         |
| <80dB(A)                     |              |              |              |            |         |
|                              | 1468 (100)   | 1098 (100)   | 370 (100)    | -          |         |
| ≥80dB(A)                     |              |              |              |            |         |
|                              | -            | -            | -            | -          |         |
| **Loudspeakers**             |              |              |              |            |         |
| <80dB(A)                     |              |              |              |            |         |
|                              | 1244 (84.7)  | 963 (87.7)   | 281 (76.0)   | <.0001     |         |
| ≥80dB(A)                     |              |              |              |            |         |
|                              | 224 (15.3)   | 135 (12.3)   | 89 (24.1)    |            |         |
| **Sound System with Headphones** |          |              |              |            |         |
| <80dB(A)                     |              |              |              |            |         |
|                              | 1304 (88.8)  | 1089 (99.2)  | 215 (58.1)   | <.0001     |         |
| ≥80dB(A)                     |              |              |              |            |         |
|                              | 164 (11.2)   | 9 (0.8)      | 155 (41.9)   |            |         |
| **Computer Games with**      |              |              |              |            |         |
| Headphones                   |              |              |              |            |         |
| <80dB(A)                     |              |              |              |            |         |
|                              | 1420 (96.7)  | 1070 (97.5)  | 350 (94.6)   | 0.01       |         |
|                      | ≥80dB(A) | <80dB(A) | ≥80dB(A) | <80dB(A) |
|----------------------|----------|----------|----------|----------|
| **Audiobooks/Program Reports** |          |          |          |          |
| ≥80dB(A)             | 48 (3.3) | 28 (2.6) | 20 (5.4) |          |
| <80dB(A)             | 1468 (100) | 1098 (100) | 370 (100) | -        |
| ≥80dB(A)             | -        | -        | -        | -        |
| **Movies with Headphones** |          |          |          |          |
| ≥80dB(A)             | -        | -        | -        | -        |
| <80dB(A)             | 1468 (100) | 1098 (100) | 370 (100) | -        |
| ≥80dB(A)             | -        | -        | -        | -        |
| **Playing an Instrument** |          |          |          |          |
| ≥80dB(A)             | 66 (4.5) | 55 (5.0) | 11 (3.0) |          |
| <80dB(A)             | 1402 (95.5) | 1043 (95.0) | 359 (97.0) | 0.10     |
| ≥80dB(A)             | -        | -        | -        | -        |
| **Playing a Second Instrument** |          |          |          |          |
| ≥80dB(A)             | 15 (1.0) | 11 (1.0) | 4 (1.1)  |          |
| <80dB(A)             | 1453 (99.0) | 1087 (99.0) | 366 (98.9) | 0.90     |
| ≥80dB(A)             | -        | -        | -        | -        |
| **Band Playing**     |          |          |          |          |
| ≥80dB(A)             | 200 (13.6) | 157 (14.3) | 43 (11.6) |          |
| <80dB(A)             | 1268 (86.4) | 941 (85.7) | 327 (88.4) | 0.20     |
| ≥80dB(A)             |          |          |          |          |
| **Classical or Opera Concert** |          |          |          |          |
| ≥80dB(A)             | -        | -        | -        | -        |
| <80dB(A)             | 1468 (100) | 1098 (100) | 370 (100) | -        |
| ≥80dB(A)             | -        | -        | -        | -        |
| **Rock, Pop, or Jazz Concert** |          |          |          |          |
| ≥80dB(A)             | 67 (4.6) | 41 (3.7) | 26 (7.0) |          |
| <80dB(A)             | 1401 (95.4) | 1057 (96.3) | 344 (93.0) | 0.01     |
|                  | <80dB(A) | ≥80dB(A) | <80dB(A) | ≥80dB(A) | <80dB(A) | ≥80dB(A) | <80dB(A) | ≥80dB(A) | <80dB(A) | ≥80dB(A) |
|------------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| 260 (70.3)       | 247 (16.8) | 137 (12.5) | 110 (29.7) |          |          |          |          |          |          |          |
| Sports Stadium   |          |          |          |          |          |          |          |          |          |          |
| <80dB(A)         | 1365 (93.0) | 1032 (94.0) | 333 (90.0) | 103 (7.0) | 66 (6.0) | 37 (10.0) |          |          |          |          |
| ≥80dB(A)         |          |          |          |          |          |          |          |          |          |          |
| Indoor Ball Sports |        |          |          |          |          |          |          |          |          |          |
| <80dB(A)         | 1347 (91.8) | 1017 (92.6) | 330 (89.2) | 121 (8.2) | 81 (7.4) | 40 (10.8) |          |          |          |          |
| ≥80dB(A)         |          |          |          |          |          |          |          |          |          |          |
| Power Tools      |          |          |          |          |          |          |          |          |          |          |
| <80dB(A)         | 1468 (100) | 1098 (100) | 370 (100) |          |          |          |          |          |          |          |
| ≥80dB(A)         |          |          |          |          |          |          |          |          |          |          |
Table S2 – DPOAE Data Presented in Figures 2 and 3. *Top, Middle,* and *Bottom* refer to the location of the graphs within Figure 3.

**Figure 2**

| Frequency (kHz) | Mean±1SD Noise Level | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value | Mean±1SD Noise Level | P-value | Mean±1SD Noise Level | P-value |
|----------------|---------------------|---------------------|---------------------|---------|---------------------|---------|---------------------|---------|
| <80 (Ref)      | 9.36 ± 4.98         | -6.04               | 8.34 ± 5.49         | -5.85   | 9.05 ± 4.60         | -6.22   | 9.55 ± 5.46         | -5.38   |
| 1.26           | 10.70 ± 5.71        | -7.45               | 9.96 ± 5.75         | -7.24   | 11.13 ± 5.10        | -7.44   | 11.45 ± 5.96        | -7.25   |
| 1.587          | 11.58 ± 5.61        | -8.46               | 10.29 ± 5.79        | -8.36   | 11.54 ± 4.45        | -8.22   | 11.89 ± 5.98        | -8.21   |
| 2              | 9.86 ± 5.78         | -9.70               | 8.27 ± 6.05         | -9.96   | 8.12 ± 5.74         | -9.98   | 10.06 ± 6.05        | -9.95   |
| 2.52           | 7.37 ± 6.03         | -10.87              | 6.51 ± 5.39         | -11.00  | 6.44 ± 5.35         | -11.11  | 7.37 ± 5.79         | -11.03  |
| 3.175          | 7.45 ± 5.89         | -11.52              | 6.84 ± 5.43         | -11.62  | 6.87 ± 5.45         | -11.71  | 6.81 ± 6.18         | -11.58  |
|        | Mean±1SD   | Noise | Mean±1SD   | Noise | P-value | Mean±1SD   | Noise | P-value | Mean±1SD   | Noise | P-value |
|--------|------------|-------|------------|-------|---------|------------|-------|---------|------------|-------|---------|
|        | (kHz)      |       | (kHz)      |       |         | (kHz)      |       |         | (kHz)      |       |         |
| 1      | 8.81 ± 5.17 | -6.49 | 8.86 ± 5.49 | -6.84 | 0.92    | 9.39 ± 4.67 | -6.80 | 0.42    | 9.52 ± 5.53 | -6.06 |
| 1.26   | 10.46 ± 5.57 | -7.89 | 9.60 ± 6.08 | -7.65 | 0.12    | 10.63 ± 5.39 | -7.69 | 0.81    | 11.62 ± 5.10 | -7.85 |
| 1.587  | 11.36 ± 5.64 | -8.79 | 10.51 ± 6.37 | -8.38 | 0.12    | 11.10 ± 5.56 | -9.12 | 0.71    | 11.98 ± 4.94 | -8.72 |
| 2      | 10.02 ± 5.66 | -10.03 | 8.90 ± 6.61 | -10.47 | 0.07    | 8.21 ± 5.79 | -10.76 | 0.01    | 10.34 ± 5.68 | -10.27 |
| 2.52   | 7.98 ± 5.74  | -11.24 | 7.16 ± 6.14 | -11.46 | 0.14    | 5.73 ± 5.61  | -11.31 | 0.002   | 7.99 ± 5.41  | -11.17 |
| Frequency (kHz) | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value<sup>a</sup> | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value |
|----------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| 1              | 9.27 ± 5.07          | -5.96                | 7.52 ± 5.93          | -5.76                | 0.09                 | 8.92 ± 5.22          | -6.48                | 8.82 ± 4.24          | -6.23                | 0.92 |
| 1.26           | 10.74 ± 5.72         | -7.41                | 7.91 ± 5.59          | -7.51                | 0.01                 | 10.53 ± 5.57         | -7.86                | 8.74 ± 5.61          | -8.48                | 0.07 |
| 1.587          | 11.50 ± 5.63         | -8.41                | 8.26 ± 5.57          | -9.15                | 0.001                | 11.34 ± 5.63         | -8.76                | 8.26 ± 5.88          | -9.77                | 0.002 |

**Figure 3**

| Final Audiometric Notch | Final Audiometric Notch |
|-------------------------|-------------------------|
| Left Ear               | Right Ear              |

| Frequency (kHz) | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value<sup>a</sup> | Mean±1SD Noise Level | Mean±1SD Noise Level | P-value |
|----------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
| 1              | 9.27 ± 5.07          | -5.96                | 7.52 ± 5.93          | -5.76                | 0.09                 | 8.92 ± 5.22          | -6.48                | 8.82 ± 4.24          | -6.23                | 0.92 |
| 1.26           | 10.74 ± 5.72         | -7.41                | 7.91 ± 5.59          | -7.51                | 0.01                 | 10.53 ± 5.57         | -7.86                | 8.74 ± 5.61          | -8.48                | 0.07 |
| 1.587          | 11.50 ± 5.63         | -8.41                | 8.26 ± 5.57          | -9.15                | 0.001                | 11.34 ± 5.63         | -8.76                | 8.26 ± 5.88          | -9.77                | 0.002 |

<sup>a</sup> P-values are based on statistical significance.
|    |        |        |        |        |        |        |        |        |        |
|----|--------|--------|--------|--------|--------|--------|--------|--------|--------|
|    | 9.66 ± 5.86 | -9.76  | 6.95 ± 6.06 | -10.31 | 0.01   | 9.86 ± 5.78 | -10.13 | 7.49 ± 5.88 | -10.98 |
| 2  | 7.26 ± 5.92  | -10.91 | 4.52 ± 6.60 | -11.87 | 0.01   | 7.80 ± 5.75 | -11.26 | 4.36 ± 5.64 | -11.81 |
| 2.52 | 7.30 ± 5.86 | -11.54 | 5.12 ± 6.71 | -11.85 | 0.05   | 7.94 ± 5.54 | -11.73 | 7.80 ± 5.35 | -11.72 |
| 3.175 | 10.28 ± 5.82 | -11.36 | 8.87 ± 7.27 | -11.27 | 0.19   | 10.67 ± 5.37 | -11.66 | 9.09 ± 6.63 | -11.82 |
| 4  | 12.86 ± 6.13 | -10.53 | 10.62 ± 6.07 | -10.79 | 0.04   | 11.15 ± 5.73 | -11.56 | 10.13 ± 6.36 | -11.51 |
| 5.04 | 7.71 ± 6.73 | -11.56 | 4.04 ± 7.41 | -12.10 | 0.004  | 6.61 ± 6.50 | -13.16 | 4.40 ± 6.17 | -13.52 |
| 6.35 |        |        |        |        |        |        |        |        |        |

*From two-sample unpaired t test.*