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Original Article

Analysis of audiometric notch as a noise-induced hearing loss phenotype in US youth: data from the National Health And Nutrition Examination Survey, 2005–2010

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Abstract

Objective: Bilateral audiometric notch (BN) at 4000–6000 Hz was identified as a noise-induced hearing loss (NIHL) phenotype for genetic association analysis in college-aged musicians. This study analysed BN in a sample of US youth. *Design*: Prevalence of the BN within the study sample was determined and logistic-regression analyses were performed to identify audiologic and other demographic factors associated with BN. Computer-simulated ''flat'' audiograms were used to estimate potential influence of false-positive rates in estimating the prevalence of the BN. *Study sample*: 2348 participants (12–19 years) following the inclusion criteria were selected from the National Health and Nutrition Examination Survey data (2005–2010). *Results*: The prevalence of BN was 16.6%. Almost 55.6% of the participants showed notch in at least one ear. Noise exposure, gender, ethnicity and age showed significant relationship with the BN. Computer simulation revealed that 5.5% of simulated participants with ''flat'' audiograms showed BN. *Conclusion*: Association of noise exposure with BN suggests that it is a useful NIHL phenotype for genetic association analyses. However, further research is necessary to reduce false-positive rates in notch identification.

Keywords: Noise, syndrome/genetics, behaviour measure, tinnitus

Introduction

Noise-induced hearing loss (NIHL) remains a hearing health concern despite national standards for hearing-protection and public health awareness campaigns. NIHL is a frequently occurring disability among current combat veterans (National Institute on Deafness ad other Communication Disorders, 2010). Several studies have found that youth are exposed to potentially hazardous levels of recreation noise which may lead to NIHL (Vogel et al, 2009; Vogel et al, 2010; Carter et al, 2014; Meinke et al, 2014). Recent reports suggest that NIHL is no longer limited to industrial workers exposed to loud noise but is found in adolescents, young adults and college-aged musicians (Phillips et al, 2010; Henderson et al, 2011).

NIHL is a complex disorder caused by the interaction of genetics and environmental factors (Kowalski et al, 2014). Complex disorders are generally defined as multiple factorial disorders because their causes are associated with multiple genes in combination with lifestyle and environmental factors (Craig, 2008). Many researchers have studied the gene-environment association of NIHL in industrial workers with the goal of developing a risk profile. Genetic variants in the metabolic enzymes important for redox regulation, heat shock protein family, gap junction proteins and ion transport proteins have been associated with NIHL (Konings et al, 2009; Pawelczyk et al, 2009; Lin et al, 2010; Sliwinska-Kowalska & Pawelczyk, 2013; Kowalski et al, 2014). However, a number of genetic associations have not been replicated in independent populations in the above listed industrial studies (Sliwinska-Kowalska & Pawelczyk, 2013). This replication failure may be attributed to the population of factory workers with age-related confounding variables, and with inconsistent use of NIHL phenotype definitions (Phillips et al, 2015; Bhatt et al, 2016)

Accurate definition of a disease phenotype is critical for improving sensitivity and specificity of genetic association analyses (Manchia et al, 2013). An audiometric notch at 3000, 4000 or 6000 Hz is identified as a characteristic of NIHL (Kirchner et al, 2012). Table 1 presents a brief summary of different notch identification criteria used in the previous research. The literature indicates that though the operational definitions of notch are

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Abbreviations

NIHL	noise-induced hearing loss
UN	unilateral notch
BN	bilateral notch
NHANES	National Health and Nutrition Examination Survey
RETSPL	reference equivalent threshold sound pressure level

variable, the notch has been widely used to report NIHL prevalence (Lees et al, 1985; Niskar et al, 2001; Phillips et al, 2010; Rawool, 2012; Mahboubi et al, 2013). In 2015, Phillips et al defined bilateral audiometric notch, most of them occurring at 6000 Hz, as a phenotype to study genetic association to NIHL. Several genetic variants of selected cochlear genes were associated with bilateral notches (BN) in a sample of college-aged musicians. It was concluded that the audiometric notch definition is a feasible NIHL phenotype for genetic association analyses.

Reliance on notches especially occurring at 6000 Hz for identifying NIHL has raised concerns (Carter et al, 2014). Elevation in hearing threshold at 6000 Hz and the subsequent appearance of a notch is attributed to error in the calibration reference value (McBride & Williams, 2001). Schlauch & Carney (2011) utilised computer simulated ''flat'' audiograms to estimate false-positive rates in reported NIHL prevalence using notch criteria described by Niskar et al (2001). The criteria were as follows: (1) thresholds at 500 and 1000 Hz ≤15 dB HL, (2) maximum threshold at 3000, 4000 or 6000 Hz ≥15 dB above the highest threshold value at 500 and 1000 Hz and (3) threshold at 8000 Hz ≥10 dB lower than the maximum threshold value for 3000, 4000 or 6000 Hz. Schlauch and Carney (2011) showed that the notch definition can lead to high false-positive rates which result in overestimation of NIHL in children and young adults.

Notch criteria utilised as a NIHL phenotype (Phillips et al, 2010, 2015) are similar to the criteria used by Niskar et al (2001) with some important distinctions. Phillips et al (2015) defined notch using the formula: ND = PT – BT, where ND is notch depth of at least 15 dB or more; PT is the poorest threshold at 4000 and 6000 Hz followed by recovery of 5 dB in hearing threshold at a subsequent high frequency; and BT is the best threshold at 1000, 2000, 3000 or 4000 Hz in a linear progression of frequencies. Unlike Niskar's definition, Phillips' definition does not include hearing threshold at 500 Hz. Instead, it utilises a linear progression of hearing thresholds at frequencies between the poorest threshold (4000 or 6000 Hz) and the best threshold (1000, 2000, 3000 or 4000 Hz). In addition, Phillips' definition includes 5 dB recovery at a subsequent high frequency following the poorest threshold at 4000 or 6000 Hz, whereas, Niskar's definition includes a 10 dB recovery at 8000 Hz. Phillips' notch identification criteria were designed to differentiate between a notch and a high-frequency hearing loss (Phillips et al, 2015; Bhatt et al, 2016). Phillips' notch definition might be susceptible to high false-positive rates especially because it includes a hearing threshold at 6000 Hz. High false-positive rates may subsequently lead to reduced sensitivity and specificity of the genetic association analyses if the notch is used as a NIHL phenotype. Therefore, it is important to estimate false-positive rates in identifying NIHL using the Phillips' notch definition.

Recent reports suggested that US youth are exposed to damaging sound levels on a regular basis (Vogel et al, 2009; Vogel et al, 2010). Almost 90% of adolescents reported that they listened to music on a regular basis, with 26% listening to music for more than 3 hours per day, and 48% of them reporting that their typical listening level was at a high or near-to-maximum volume (Vogel et al, 2009; Vogel et al, 2010). Personal music players have been shown to exceed damaging sound pressure levels at high volume control settings (Breinbauer et al, 2012). Research on the auditory lifestyle of college students has showed that almost 50% were exposed to potentially harmful music, 44% used noisy equipment without hearing-protection and almost 29% of them worked in a noisy environment (Rawool & Colligon-Wayne, 2008). However, the current literature is not conclusive about the effects of recreational acoustic exposure on hearing (Carter et al, 2014). Therefore, it is important to study the prevalence of the BN defined as a NIHL phenotype in the previous study (Phillips et al, 2015) and its associated factors in US youth (12–19 years) with the goal of profiling non-genetic risk factors of NIHL.

The present study had two goals. The first goal was to review the hearing database from the National Health and Nutrition Examination Survey (NHANES) from 2005–2010, and report prevalence and association factors of the notch in a sample of US youth (12–19 years). The second goal was to use computer

Table 1. A brief summary of audiometric notch identification criteria used in previous research.

Study	*Notch identification criteria*
Mahboubi et al (2013)	(1) 4 kHz threshold ≥25 dB HL, (2) 4 kHz threshold ≥10 dB compared to the 2 kHz threshold and (3) 4 kHz threshold ≥10 dB compared to the 8 kHz threshold.
Phillips et al (2010)	ND = PT – BT, where (1) ND is notch depth of at least 15 dB or more, (2) PT is the poorest threshold at 4000 and 6000 Hz followed by recovery of 5 dB in hearing threshold at subsequent high frequency and (3) BT is the best threshold at 4000, 3000, 2000 or 1000 Hz in a linear progression of frequencies
Agrawal et al (2008)	Absolute hearing threshold values: it was defined as high-frequency hearing loss with a pure-tone mean of 25 dB or higher at 3, 4 and 6 kHz
Hoffman et al (2006)	(1) Threshold worse by ≥15 dB at 3, 4 or 6 kHz than the average thresholds at 0.5 and 1 kHz and (2) 8 kHz threshold ≥5 dB than the worse threshold at 3, 4 or 6 kHz
Dobie & Rabinowitz (2002)	(1) Notch depth of ≥0 dB, where notch depth was calculated by subtracting the average thresholds at 1 and 8 kHz from the average thresholds at 2, 3 and 4 kHz.
Niskar et al (2001)	(1) 0.5 and 1 kHz thresholds ≤15 dB HL, (2) Threshold worse by ≥15 dB at 3, 4 or 6 kHz than the thresholds at 0.5 and 1 kHz and (3) 8 kHz threshold ≥10 dB than the worse threshold at 3, 4 or 6 kHz
McBride and Williams (2001)	(1) V-shaped notch of ≥15 dB occurring at one audiometric frequency or (2) U-shaped notch occurring at more than one audiometric frequencies with the notch depth of ≥20 dB and ≥10 dB recovery at the high frequency
Coles et al (2000)	(1) Threshold worse by ≥10 dB at 3, 4 or 6 kHz than those at 1 or 2 kHz and 6 or 8 kHz
Lees et al (1985)	(1) 10 dB depression of hearing threshold below the audiometric frequencies on both sides

simulation in conjunction with the NHANES 2005–2010 data to demonstrate the likely contribution of measurement variability to the percentage of audiograms identified as having audiometric notches using the criteria described by Phillips et al (2015).

Materials and methods

NHANES database for the study

Audiometric testing was performed as an annual, ongoing, cross-sectional survey by health technicians at a mobile examination centre of the National Center for Health Statistics. Data were collected through household interviews followed by standardised physical examinations. Demographic and audiometric databases from NHANES 2005–06, 2007–08 and 2009–10 were downloaded from the NHANES website (http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm) and a combined database was formed. Data were extracted for the age group of 12–19 years.

Audiometric measures

An interacoustic model AD226 audiometer (Interacoustics, Eden Prairie, MN) with standard TDH-39 headphones was used to measure hearing sensitivity. Hearing thresholds in the test ear were measured using Etomotic EarTone 3A (Etymotic, Elk Grove Village, IL) insert earphones if the observed hearing threshold at any given frequency was poorer than the non-test ear threshold by 25 dB at 500 and 1000 Hz; or 40 dB at any higher frequency. Output calibration checks and an environmental noise survey were conducted at each site before testing. A modified Hughson–Westlake procedure with 5 dB step-size was followed using the automated testing mode of the audiometer. The effective range for automated audiometric testing was from –10 to 100 decibels (dB) at 500 to 6000 Hz and –10 to 90 dB at 8000 Hz. Thresholds were tested through 120 dB (110 dB at 8000 Hz) using the manual audiometric mode. Observed values, therefore, varied between –10 and 120 dB HL. Manual testing was also conducted when the examinee could not operate the response switch or responded too slowly for the audiometer to accurately record the response. The 1000 Hz frequency was tested twice in each ear as a measure of reliability of the participant's responses. Tympanometry was conducted using an Earscan acoustic impedance tympanometer (Micro Audiometrics, Murphy, NC) in a sound-treated room at a mobile examination centre. Additional information about the data collection procedure can be found on the NHANES website: http://www.cdc.gov/nchs/nhanes/nhanes_questionnaires.htm.

Study population

Demographic and audiometric data were extracted for the age group 12–19 years from the combined database. Individuals with bilateral normal otoscopic findings, tympanometric compliance value ranges from 0.2 to 1.8 cc and middle ear pressure values from –50 to 25 dapa in both ears were considered for further analysis. These inclusion criteria were applied to the NHANES data to prepare a subset database equivalent to Phillips et al (2010, 2015). A total of 2348 participants met the inclusion criteria. Their hearing thresholds were analysed to report the prevalence of the audiometric notch.

Demographic and audiological data

Age of the participants was categorised in three subgroups: 12–13 years, 14–15 years, 16–17 years and 18–19 years. Race/ethnicity was re-coded into non-Hispanic European American, non-Hispanic African American, Hispanic and other races (including multiracial). Socioeconomic status was estimated from the poverty/income ratio (PIR) in three categories: low (PIR $\leq$1.3), middle (PIR from 1.4 to 3.5) and high (PIR more than 3.5). Work-related noise exposure was defined as positive if a participant answered positively to the question, ''Have you ever had a job where you were exposed to loud noise for five or more hours a week?''. Recreational acoustic exposure was defined as positive if a participant identified exposure to loud noise or music for five or more hours per week outside of a job. Acoustic exposure before testing was defined as positive if a participant indicated exposure to loud music or noise in the last 24 hours. Firearms noise exposure was considered positive if a participant answered positively to the question, ''Have you ever used firearms for target shooting, hunting or for any other purposes?''. Tinnitus was coded as positive if a participant answered positively to the question. ''In the past 12 months, have you been bothered by ringing, roaring or buzzing in your ears or head that lasted for five minutes or more?''. Although 2348 participants met the inclusion criteria, 259 participants were missing demographic or audiological data. These participants were excluded, and the regression analyses were performed on 2089 participants with complete data.

Audiometric notch

Audiometric notch was defined using the formula: ND = PT – BT, where ND is notch depth of at least 15 dB or more; PT is the poorest threshold at 4000 and 6000 Hz followed by recovery of 5 dB in hearing threshold at subsequent high frequency; and BT is the best threshold at 4000, 3000, 2000 or 1000 Hz in a linear progression of frequencies (Figure 1; Phillip et al, 2010, 2015). Participants were classified into three groups using this definition: no notch (NN), unilateral notch (UN) and bilateral notch (BN). A 4000 Hz or 6000 Hz notch was identified when the poorest threshold was obtained at 4000 Hz or 6000 Hz, respectively. A notch was considered unspecified when the poorest threshold at 4000 Hz and 6000 Hz was equal.

Computer simulations

Computer simulations were performed in R language (Ihaka & Gentleman, 1996) using the method described by Schlauch and Carney (2011). Audiograms for 3000 simulated listeners were generated. The process has four steps. In the first step, the physiological thresholds or simulated listener's ''actual'' thresholds were selected from a simulated Gaussian distribution with a mean of 0 dB and SD of 7.5 dB. The Gaussian distribution was allowed to truncate from the negative side (cutoff = -10 dB HL) to simulate measurement bias of a conventional audiometer as they do not measure hearing thresholds below -10 dB HL. A randomly selected value from the distribution was considered ''actual'' hearing threshold of a listener in both ears at 1000, 2000, 3000 and 4000 Hz. At 6000 and 8000 Hz, a 5-dB correction factor was added to the selected value from the distribution to derive ''actual'' hearing threshold at 6000 and 8000 Hz. The correction factor was added to mimic measurement bias observed at the high frequencies in the NHANES data (Schlauch & Carney, 2011). In the second step, an audiogram was generated based on known limitations of the precision of puretone audiometry (Schlauch & Carney, 2011). ''Sensory'' thresholds at audiometric frequencies 1000, 2000, 3000,

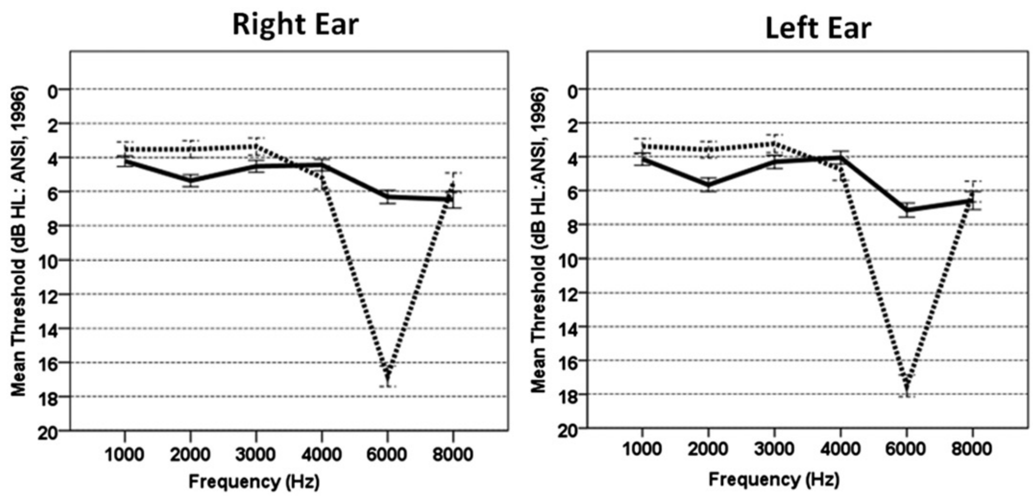

Figure 1. Audiometric Notch Configuration in the NHANES (2005–2010) database: Mean thresholds at 1000–8000 Hz for participants with no notch (solid line) versus notched audiogram (dashed line line). Error bars indicate 95% confidence interval.

4000, 6000 and 8000 in both ears were selected randomly from Gaussian distributions centred on the simulated person's ''actual'' threshold at each frequency with a SD of 5 dB. In the third step, all ''sensory'' thresholds obtained from the Gaussian distribution surrounding the ''actual'' thresholds were rounded to the nearest 5 dB value as audiometric thresholds are measured using 5 dB steps. Finally, in the fourth step, threshold values lower than -10 dB HL was rounded to -10 dB HL as most commercially available audiometers cannot obtain hearing thresholds lower than -10 dB HL. Further details of the computer simulation can be found in Schlauch & Carney (2011).

Statistical analysis

The prevalence of NN, UN and BN was calculated among total participants between the ages of 12–19 years, and within various socio-demographic characteristics, noise exposure and hearing-related factors. Gender, age, ethnicity, income, work-related noise exposure, recreational acoustic exposure, acoustic exposure before testing, firearms noise exposure and tinnitus were defined as independent variables. Multinomial logistic regression was used to calculate the odds ratio for each independent variable after statistical adjustment for all others was made. A logistic regression analysis was performed on 2089 participants with complete data for all the dependent variables listed above. A chi-square test of independence was performed to determine the differences in the prevalence of notches in the NHANES data and the computer simulated data. A *post hoc* cellwise analysis with adjusted residuals (2×3 model) was performed to identify the source of significance in the chi-square test (García-pérez & Núñez-antón, 2003). Statistical analyses were performed using the IBM SPSS Statistics 23.0 for Windows (IBM Software Group. Chicago, IL).

Results

Audiologic/otologic descriptor

The overall prevalence of audiometric notch in at least one ear was 55.6% in the entire study sample of 2348 participants. Among the entire study sample, 390 individuals (16.6%) showed BN; 915 individuals (39%) showed UN and 1043 individuals (44.4%) showed NN (Supplement A). Among the participants with BN, 82% revealed the 6000 Hz notch and 4.3% revealed the 4000 Hz notch in both ears. Almost 29.4% and 33.6% of the participants in the entire study sample showed the 6000 Hz notch in the right and left ears, respectively. Similarly, almost 5.3% and 6% of the participants in the entire study sample showed the 4000 Hz notch in the right and left ears, respectively. The notch depth analysis showed that almost 42%, 29.5% and 28.5% of the participants with the 6000 Hz notch in the right ear revealed notch depth of 15, 20 and ≥25 dB, respectively. Similarly, almost 39.8%, 30.7% and 29.5% of the participants with the 6000 Hz notch in the left ear revealed notch depth of 15 dB, 20 dB and ≥25 dB, respectively.

Questionnaire data

The study sample consisted of 2348 participants ranging in age from 12 to19 years (Supplement A). Among them, 507 (23.7%) were aged 12–13 years, 598 (25.5%) were aged 14–15 years, 632 (26.9%) were aged 16–17 years and 561 (23.9%) were aged 18–19 years. This sample included 1074 (45.7%) males and 1274 (54.3%) females. Ethnicity of the study sample was categorised in four groups: 721 (30.7%) were European American (non-Hispanic), 648 (27.6%) were African American (non-Hispanic), 852 (36.3%) were Hispanic and 127 (5.4%) were from other races or multiracial. Family income was classified into three groups: 510 (21.7%) showed high income, 779 (33.2%) showed mid income and 894 (38.1%) showed low income. Almost 7% of individuals reported that they had a noisy job were they were exposed to loud noise for five or more hours a week. Recreational acoustic exposure was reported by almost 22.5% of participants showing that they were exposed to steady loud noise or music for five or more hours a week outside of their job. Almost 37.7% reported that they were exposed to loud music or noise in the past 24 hours before testing. Almost 7% of individuals reported that they were bothered by ringing, roaring or buzzing in their ears or head that lasted for 5 minutes or more. Among the study sample, 361 (15.4%) reported that they used firearms for target shooting, hunting, or for any other purposes. Almost 41.5% of the study sample reported a history of active or passive smoking.

Results of logistic regression analysis

Logistic regression analysis revealed that males showed lower prevalence of BN compared to females [odds ratio (OR): 0.585 (95% CI: 0.450–0.761), $p = 0.00006$]; individuals with African American non-Hispanic ancestry showed lower prevalence of BN compared to individuals with European American non-Hispanic ethnicity [OR: 0.537 (95% CI: 0.376–0.767), $p = 0.001$]; and individuals with work-related noise exposure showed more prevalence of BN compared to individuals without work-related noise exposure [OR: 1.836 (95% CI: 1.097–3.074), $p = 0.021$] (Supplement B). The analysis further revealed that males showed lower prevalence of UN compared to females [OR: 0.753 (95% CI: 0.618–0.918), $p = 0.005$]; individuals with African American non-Hispanic ethnicity showed lower prevalence of UN compared to individuals with European American non-Hispanic ethnicity [OR: 0.700 (95% CI: 0.538–.911), $p = 0.008$]; individuals aged 14–15 years showed significantly higher prevalence of UN compared to individuals aged 18–19 years [OR: 1.333 (95% CI: 1.005–1.769), $p = 0.042$]. In addition, males showed lower prevalence of the overall notch (bilateral and unilateral combined) compared to females [OR: 0.7 (95% CI: 0.584–0.839), $p = 0.0001$]; participants with African American ancestry showed lower prevalence of the overall notch [OR: 0.650 (95% CI: 0.510–0.829), $p = 0.001$]. No other factors included in the analysis revealed a significant relationship with the notch (Supplement B).

Results of computer-simulated audiograms

Figure 2 compares prevalence of audiometric notch between the NHANES (2005–2010) database and computer-simulated database. Computer simulation captured many characteristics of the NHANES (2005–2010) database as shown by Figure 3. Descriptive statistics revealed that 63.7% of simulated individuals showed NN, 30.8% of them showed UN and 5.5% showed BN. Among the BN, 82.9% showed the 6000 Hz notch and 17.1% showed the 4000 Hz notch in the right ear. Almost 82.3% showed the 6000 Hz notch and 17.7% showed the 4000 Hz notch in the left ear. Simulated data revealed that 17.5% and 17.3% of participants showed the 6000 Hz notch in the right and left ears, respectively. Almost 3.3% and 3.6% of the simulated participants showed the 4000 Hz notch in the right and left ears, respectively. A chi-square test and a cellwise *post hoc* test revealed that the prevalence of BN within the US youth sample (16.6%) was significantly higher than the prevalence of BN (5.5%) in the simulated data ($X^2 = 198.27$, $p < 0.0001$). Similarly, the prevalence of UN among the US youth sample (39%) was significantly higher than the prevalence of UN (30.8%) in the simulated data ($X^2 = 38.71$, $p < 0.001$).

Discussion

Prevalence of audiometric notch and associated factors

The major finding of this study is that the overall prevalence of the 4000–6000 Hz notch was 55.6% across the study sample. Almost 16.6% showed BN utilised as a NIHL phenotype in a previous study (Phillips et al, 2015). Our results revealed that individuals with a noise exposure history showed significantly high prevalence of BN. This finding supports the previous report that the BN is a feasible NIHL phenotype to study genetic association in the population of young adults (Phillips et al, 2015). In addition, females with European American non-Hispanic ethnicity and with history of a noisy job exhibited significantly high odds of showing BN.

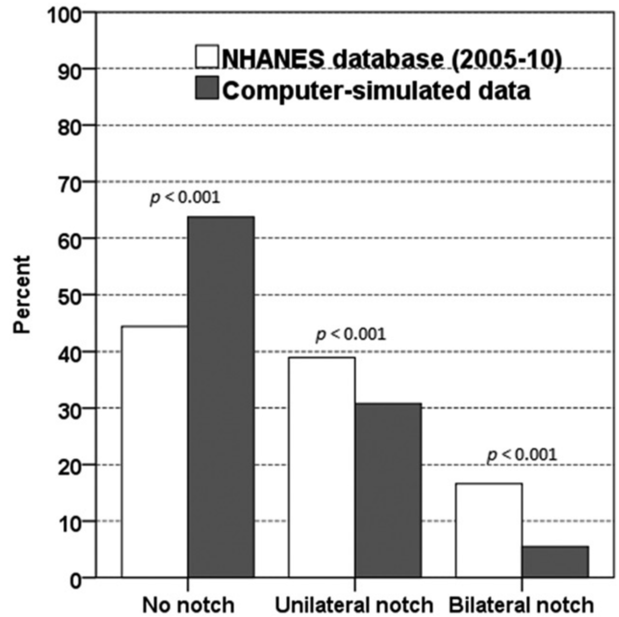

Figure 2. Percentage of no notch, unilateral notch and bilateral notch audiograms in NHANES (2005–2010) database (empty bars) versus computer-simulated ''flat'' audiogram database (gray bars). *p* values describe statistical significance in the *post hoc* cellwise analysis in the 2 × 3 contingency table. *p* values suggest that individuals with no notch are significantly higher and individuals with UN and BN are significantly lower in the computer simulated database compared to the NHANES database (2005–10).

These findings are in agreement with previously published reports on NIHL prevalence data (Ishii & Talbott, 1998; Lin et al, 2011; Mahboubi et al, 2013). A previous study associated rising prevalence of high-frequency hearing loss in females with lower prevalence of hearing-protection use compared to males (Henderson et al, 2011). This may be a factor in observing significantly high prevalence of notches in females.

Audiometric notch and acoustic exposure

Literature is lacking conclusive evidence on effects of recreational noise exposure on hearing (Carter et al, 2014). Our analysis revealed no association to recreational acoustic exposure and BN after statistically controlling for the effects of other variables. This result may be attributed to the study population which might be too young to show the effects of cumulative recreational acoustic exposure on hearing. Audiometric thresholds may not be sensitive enough to identify subtle damage to the auditory system due to recreational acoustic exposure in this population (Attias et al, 2001). Additionally, the NHANES survey design might have influenced the results of our statistical analysis as the survey questions might have limitations in estimating recreational acoustic exposure.

We compared our results with Phillips et al (2010) as they utilised the same notch definition to report NIHL prevalence in college-aged musicians. A chi-square test (2 × 3 model) and a cellwise *post hoc* test were performed to determine differences in the prevalence of BN in the NHANES data and in the data of student musicians. Results revealed that the prevalence of BN among the sample of US youth (16.6%) was significantly higher than the prevalence of BN (11.5%) in student musicians ($X^2 = 8.93$,

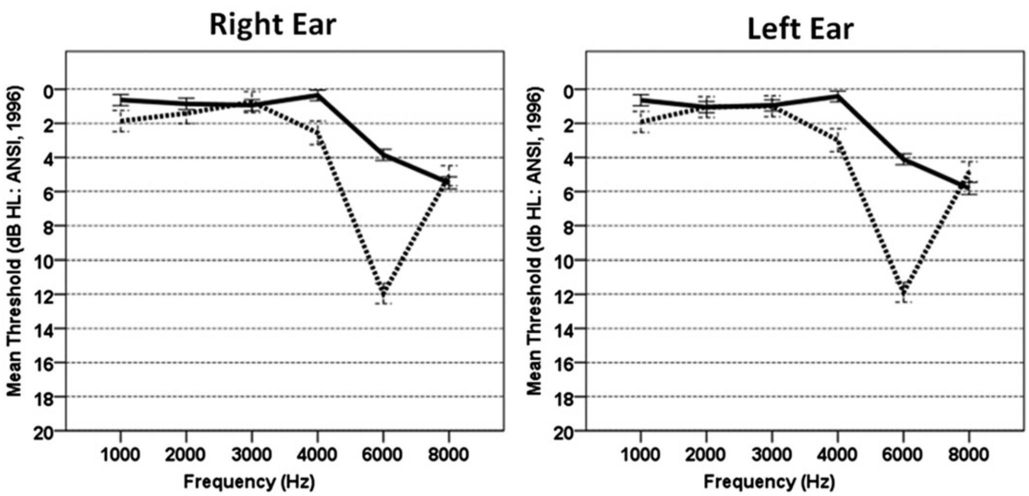

Figure 3. Audiometric 4000–6000 Hz notch configuration in the computer-simulated database: Mean thresholds at 1000–8000 Hz for simulated participants with no notch (solid line) versus notched audiogram (dashed line line). Error bars indicate 95% confidence interval.

$p < 0.01$). Similarly, UN showed higher prevalence (39%) in the sample of US youth compared to the prevalence (33.5%) reported in the sample of young musicians ($X^2 = 8.46$, $p < 0.01$). Therefore, we concluded that high prevalence of notches in the sample of US youth cannot be attributed merely to frequent exposure to loud recreational noise or music.

Evidence of high false-positive rates

The percentage of audiometric notches in the computer simulated ''flat'' audiograms is an estimate of the false-positive rate in the NHANES (2005–2010) database. Almost 36.3% simulated individuals with ''flat'' audiograms showed the notch in at least one ear, and 5.5% showed BN. Figure 4 shows the 6000 Hz notch depth as a function of the percentage of notched audiograms in the computer-simulated data and NHANES (2005–10) data. Among the simulated participants with the 6000 Hz notch in the right ear, almost 65.3% showed 15 dB of notch depth, 27.8% showed 20 dB of notch depth and 6.3% showed $\geq$25 dB of notch depth (Figure 4). Similarly, among the simulated participants with the 6000 Hz notch in the left ear, almost 64.6% showed 15 dB of notch depth, 27.1% showed 20 dB of notch depth and 8.3% showed $\geq$25 dB of notch depth. A chi-square test and a cellwise *post hoc* test were performed to identify differences between notch depth in NHANES data and in the computer-simulated data. Results of the analysis are summarised in Figure 4. Our results suggested that the false-positive rates in identifying audiometric notches were high and might affect the genetic association analyses if the BN is treated as the NIHL phenotype. We concluded that the notch identification criteria need to be stringent to accommodate for the variability in hearing threshold measurements to reduce the high false-positive rates.

Audiometric notch and standing waves in the ear canal

Standing waves in the ear canal has been proposed to influence baseline audiometric thresholds and temporary threshold shift (TTS) (Gerhardt et al, 1987; Dirks et al, 1996; Lawton, 2005). Ear canal length, and consequently its resonance frequency, has been associated with the pattern of audiometric notch in the baseline audiogram (Gerhardt et al, 1987; Dirks et al, 1996). Individuals with shorter ear canal have been shown to exhibit greater variation in the reference equivalent threshold sound pressure levels (RETSPL) which might result in false notch at high frequencies, even for otologically normal young persons (Dirks et al, 1996;

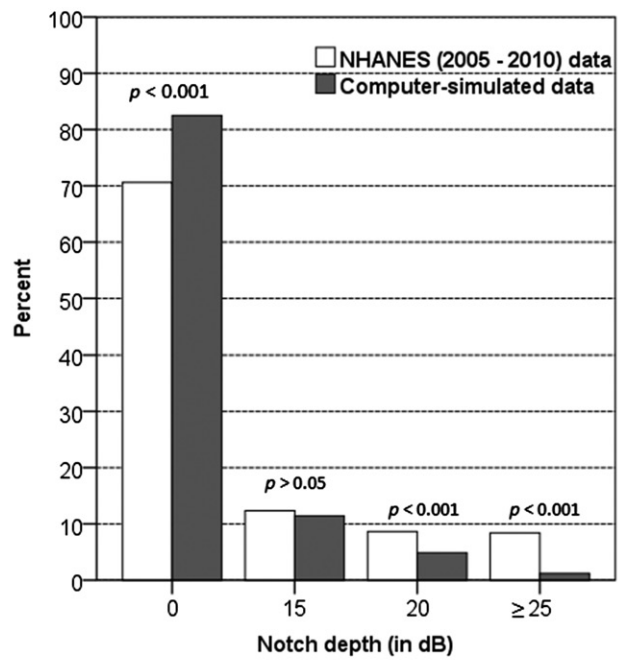

Figure 4. Depth of audiometric notch at 6000 Hz as a function of percentage of notched audiograms in the computer-simulated data versus NHANES (2005–10) data. Data from both ears are combined. p values describe statistical significance in the *post hoc* cellwise analysis in the 2×4 contingency table. p values suggest that individuals with no notch (0 dB notch depth) are significantly higher in the computer simulated data compared to the NHANES (2005–10). No significant difference was obtained in the prevalence of the 6000 Hz notch with 15 dB notch depth between the both databases. The prevalence values of the 6000 Hz notch with 20 dB and $\geq$25 dB notch depth were lower in the computer simulated data compared to the NHANES (2005–10).

Lawton, 2005). Younger participants in this study might have a shorter ear canal and subsequently show higher prevalence of audiometric notches. Ear canal length has been associated with the pattern of TTS. Individuals with a smaller ear canal showed a notch at 6000 Hz and individuals with a longer ear canal showed a notch at 3000 Hz followed by identical noise exposure (Gerhardt et al, 1987). These results suggested that standing waves in the ear canal might influence high false-positive rates of notches in the NHANES (2005–2010) data.

Possible solutions to reduce false-positive rates

Schlauch and Carney (2011) argued that notch definitions which weigh 6000 Hz hearing thresholds equally with other frequencies tend to show high false-positive rates. Thresholds at 6000 Hz are more variable than those of lower frequencies when TDH-style earphones are used (Arlinger, 1991; Schlauch & Carney, 2007). We calculated the overall prevalence of the 6000 Hz notch as a function of notch depth in the NHANES (2005–10) data and in the computer simulated data. Almost 29.4% and 17.5% of audiograms showed $\geq$15 dB notch depth at 6000 Hz in the NHANES (2005–10) database and in the simulated database, respectively. If the notch depth criterion is modified to control for the high false-positive rates, from notch depth of $\geq$15 dB to $\geq$25 dB, then almost 8.4% and 1.2% of audiograms identified with the 6000 Hz notch in the NHANES (2005 – 10) database and in the simulated database, respectively. This observation implies that deeper notches may be less prone to high false-positive rates suggesting that 6000 Hz should be weighted differently than the others to reduce false-positive rates. However, stringent notch definitions with high notch depth criteria might not be useful in the genetic association analyses as they might compromise sensitivity of the phenotyping process in identifying early indications of NIHL.

Another possible way to reduce false-positive rates is by reducing variability in the hearing threshold at 6000 Hz. A majority of studies exploring NIHL prevalence, including Phillips et al (2010, 2015) and NHANES (2005–10), used supra-aural headphones for measuring hearing thresholds. These headphones showed high SDs in the RETSPL at 6000 Hz for normal hearing individuals (Arlinger, 1991; Lutman & Davis, 1994). High SD values in the RETSPL resulting from individual variation in outer ear resonance may result in notch-like audiometric configuration (Arlinger, 1991; Lawton, 2005). Insert earphones would be a good choice to study the prevalence of NIHL in young populations as they are likely to reduce variability in RETSPL by eliminating concha resonance and the possibility of collapsed ear canals (Schlauch & Carney, 2007; Schlauch & Carney, 2011).

Limitations of the study

The NHANES estimates acoustic exposure and other related factors included in the analysis through a questionnaire-based research design. Validity of this questionnaire is not well documented which might influence our results of the regression analysis. The inclusion criteria of middle ear pressure ranging from −50 to 25 dapa may be restrictive and it may exclude several participants with a clinically normal functioning middle ear (ASHA, 1990). In addition, this study utilised the computer-simulation technique described by Schlauch & Carney (2011) to estimate potential influence of false-positive rates in the identification of audiometric notches at 4000–6000 Hz. Our results might be influenced by the computer simulation technique which required a series of assumptions to generate the ''flat'' audiograms. All of the assumptions made for the simulations have not been validated (e.g. assumption of independence of hearing thresholds at different frequencies and assumption of the configuration of the ''flat'' audiogram). Results of the regression analysis might not be generalised directly to the non-institutionalised population of US youth aged 12–19 years as the analysis was performed on an unweighted sample.

Future research directions

The current study identified the necessity of refining the audiometric testing procedure to improve accurate identification of a NIHL phenotype for the genetic association analysis. We hypothesised that standing waves in the ear canal is a candidate mechanism underlying the high false-positive rates observed in our study. Standing waves may produce a small deviation in the real-ear threshold sound pressure levels from the RETSPL at 6000 Hz. The error in sound pressure level across the audiometric frequency range may mimic a notch-like configuration in the absence of cochlear damage. Further research is needed to test this hypothesis with the goal to improve identification of notch for genetic association analyses.

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Supplementary material available online