Influences of GST polymorphisms to music-induced hearing impairment

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ABSTRACT

Introduction:

Both genetic and environmental factors contribute to noise-induced hearing loss (NIHL). The objective of this study is to investigate the hypothesis that Glutathione S-transferase (GST) genetic polymorphisms was related to susceptibility to developing NIHL caused by music exposure.

Methods:

This cross-sectional study recruited high school students who habitually listen to music with portable players. PTA, distortion product otoacoustic emission (DPOAE), and questionnaire were obtained. Cumulative noise exposure (CNE) was calculated by listening time and volume of using portable players. Effects of GST1, GSTM1 and GSTP1-105 on NIHL were analyzed.

Results:

A total of 312 subjects were analyzed. Mean of PTA for high frequencies (average of 3k, 4k and 6k Hz) was 8.07 dB HL (SD = 5.98). DPOAE amplitude level for high frequencies was 20.28 dB SPL (SD = 5.10). Mean of CNE was 84.57 dB-year (SD = 11.42). With the regression analysis model, there was a good dose-response relationship between CNE and DPOAE amplitude levels for high frequencies ($p < 0.05$). Furthermore, those subjects, with GSTT1-null, GSTM1-null and GSTP1-105 Ile/Ile genotypes, had higher susceptibility for developing otoacoustic emission levels reduction for high frequencies ($p < 0.05$).

Conclusions:

This study identified that GST genetic polymorphisms might modify the susceptibility of hearing impairment for high frequencies caused by MP3 player exposure. Moreover, investigations of other genotypic variants involved in oxidative stress response for elucidating the gene-environment interaction for NIHL are warranted

Keywords:

Noise induced hearing loss, Teenager, Glutathione S-transferase, genetic polymorphism

INTRODUCTION

Noise-induced hearing loss (NIHL) is a significant public health problem. It is well known that exposure to excessive noise for long durations can cause a significant NIHL. In recent years, the popularity of portable digital music players, such as MP3 players, has increased substantially and may now represent one of the most common types of leisure noise exposure. Millions of adolescents and young adults are potentially at risk of permanent hearing loss through listening to their favorite music.

Excessive noise exposure can lead to metabolic and/or mechanical effects resulting in alterations of the structural elements of the organ of Corti. The primary damage is concentrated on the outer hair cells. Otoacoustic emissions (OAEs) are thought to reflect the nonlinear active processes of the cochlea based on the motile activity of the outer hair cells. In noise-exposed individuals, OAEs may be decreased even before changes in audiometric thresholds occur. As such they can provide an 'early warning' of outer hair cell damage.

NIHL is a complex disease that is caused by interactions between environmental and genetic factors. The generation of reactive oxygen species (ROS) is believed to be an important factor associated with tissue destruction through metabolic stress. Since antioxidants can scavenge and eliminate the damaging ROS, antioxidants may interrupt the apoptotic biochemical cascade that results in the death of irreplaceable hair cells. The antioxidant enzymes involved in glutathione (GSH) metabolism include glutathione S-transferase (GST), glutathione peroxidase (GPX1), and glutathione reductase (GSR). According to the findings of previous research, mutations in all three GST genes (i.e. GSTT1, GSTM1 and GSTP1) are known to result in oxidative stress, the retention of reactive quinone intermediates in cells, and the progression of cell death. Our own prior research found that male workers carrying all genotypes of GSTT1 null, GSTM1 null and GSTP1 Ile105/Ile105 were susceptible to noise-induced hearing threshold levels for high frequencies.

The objective of this study is to investigate the hypothesis that GST genetic polymorphisms was susceptible to developing music-induced otoacoustic emission levels for high frequencies (OAEHF) caused by MP3 player exposure.

METHODS AND MATERIALS

This cross-sectional study recruited high school students who habitually listen to music with MP3 players. At the beginning of the study, an interview using a

standard questionnaire was conducted concerning noise exposure, mobile phone use, smoking, alcohol use, drug history, middle ear disease and congenital deafness. A previous otoscopic exam determined study eligibility. Pure-tone audiometry (PTA), distortion product otoacoustic emission (DPOAE), and questionnaire were obtained. Cumulative noise exposure (CNE) was calculated by listening time and volume of using MP3 players. Deletion polymorphisms in the GSTT1 and GSTM1 genes, and single nucleotide polymorphism (Ile -105 Val) in GSTP1 were determined by polymerase chain reaction-based methods. Those subjects with GSTM1-null, GSTT1-null, and GSTP1 Ile105/Ile105 were considered to have poor oxidative genotypes. Statistical analysis was performed to evaluate the relation between CNE of MP3 player and noise-induced PTA / DPOAE levels for high frequencies (average threshold level of 3k, 4k, and 6k Hz) (PTA_H3, OAE_H3), with the different genetic variants of GSTT1, GSTM1, and GSTP1.

Inclusion criteria

1) High school students (girl, 13-18 years old)
2) Habitually listening to music with MP3 players

Exclusion criteria

1) Conductive or mixed hearing impairment (middle ear disease)
2) Family history of congenital deafness
3) Mental retardation
4) High noise exposure before 24 hours
5) Previous history of noise exposure (e.g. musician)
6) Overuse of a mobile phone (frequency, duration) (>60 minutes / day)

Cumulative noise exposure (CNE)

1) Hypothesis: noise could damage the hearing system cumulatively
2) Parameters:
(a) Estimated output levels (dB) of portable music players (Leq)
(b) Listening time (hours / week), average in the past 2 years (Thour)
(c) Total years of habitually listening to music with MP3 players (Tyear)
3) Equation:

$$CNE = 10 \cdot \log [Thour \cdot Tyear \cdot 10^{(Leq/10)}]$$

RESULTS

A total of 312 subjects were analyzed (table 1). The average age was 16.97 years. Mean of PTA for high frequencies (PTA_H3) was 8.07 dB HL (SD = 5.98). DPOAE amplitude level for high frequencies (OAE_H3) was 20.28 dB SPL (SD = 5.10). Mean of CNE was 84.57 dB-year (SD = 11.42). Sixty-nine

subjects (22.11%) harboring all three genotypes (GSTM1 null, GSTT1 null and GSTP1 Ile105/Ile105) were presumed to have poor antioxidant capability. Under the univariate regression analysis, none of the following variables was found to be significantly associated with PTA_H3: age, smoking, drinking alcohol, use of a mobile phone, CNE of music and GST antioxidant capability (table 2). With the regression analysis model, there was a good dose-response relationship between CNE and DPOAE amplitude levels for high frequencies ($p = 0.038$) (table 3).

Furthermore, those subjects, with GSTT1-null, GSTM1-null and GSTP1-105 Ile/Ile genotypes, had higher susceptibility for developing otoacoustic emission levels reduction for high frequencies ($p = 0.027$) (figure 2).

Conclusions

In our study, total noise exposure was an important component of the assessment. In practice it is difficult to estimate noise exposure amounts over time with MP3 player.

Similar to previous studies, we found that OAEs could be used to assess existing subclinical outer hair cell change and preclinical frequency-specific hearing loss. We found that girl students with GSTM1 null, GSTT1 null and GSTP1 Ile105/Ile105 genotypes had a relatively poor high-frequency hearing, after the long-term exposure of MP3 player.

Further studies in this area could benefit from an increased sample size, investigations of other genotypic variants involved in the cell antioxidant system (e.g. GPX, GSR, CAT, and superoxide dismutase), and long-term follow up.

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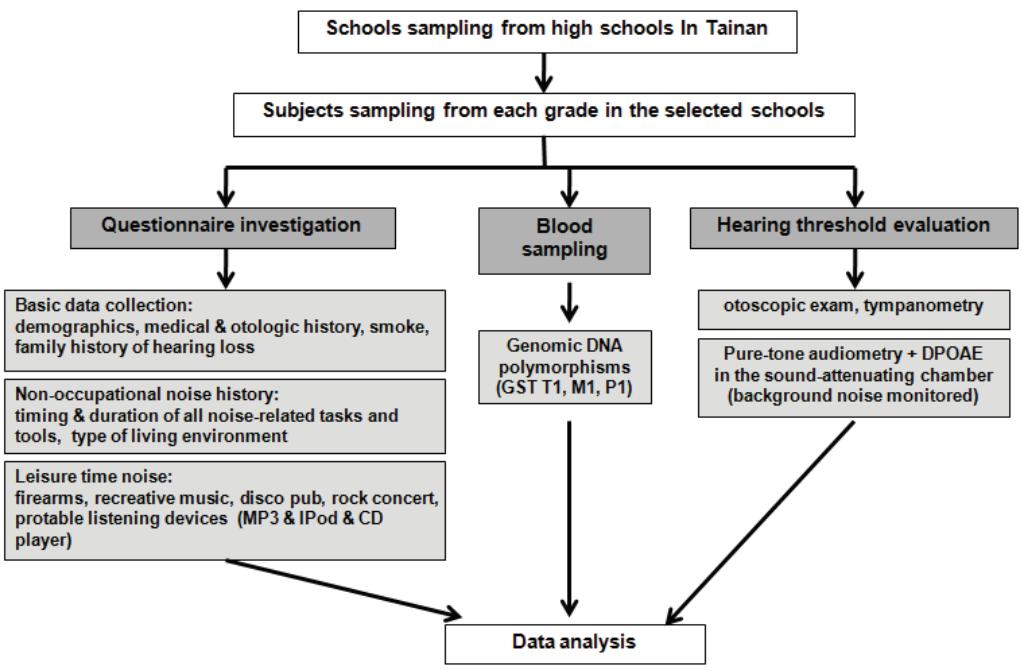

Figure 1. Study protocol of our study.

Variables	Mean (SD)	Number (%)
Age (years)	16.97 (0.97)	
Smoking (yes)		11 (3.73%)
Drinking alcohol (yes)		8 (2.56%)
Use of a mobile phone (yes)		279 (89.42%)
amount of time mobile phone used (minutes/ day)	14.01 (14.98)	
Cumulative exposure amount of music (dB SPL)	84.57 (11.42)	
estimated output levels of MP3 players (dB SPL)	57.99 (8.19)	
amount of time listening to music (hours/week)	5.14 (6.53)	
time of habitually listening with MP3 player (years)	3.81 (2.17)	
GST genetic polymorphism		
GST P1-105: Ile-Ile		203 (65.06%)
GST T1: Null		157 (50.32%)
GST M1: Null		192 (61.54%)
Antioxidation capability: Poor		69 (22.11%)
Antioxidation capability: Normal		243 (77.89%)
Pure tone hearing threshold level (PTA_H3)(dB HL)	8.07 (5.98)	
DPOAE amplitude level (OAE_H3) (dB SPL)	20.28 (5.10)	

Table 1. Demographic and personal characteristics (N=312, girls)

Variables	PTA threshold level (PTA_H3)		
	β / mean	R^2	*p*-value
Age (years)	0.655	0.011	0.061
Smoking: Yes	8.151	0.004	0.239
No	5.985		
Drinking alcohol: Yes	8.122	0.002	0.383
No	6.250		
Use of a mobile phone: Yes	8.611	0.001	0.586
No	8.011		
Cumulative exposure amount of music	0.046	0.009	0.103
GST antioxidation capability			
poor	8.162	0.001	0.628
normal	7.766		

Table 2. Univariate regression analysis of PTA threshold levels for high frequencies (PTA_H3)

Variables	DPOAE amplitude level (OAE_H3)		
	β / mean	R^2	*p*-value
Age (years)	-0.466	0.008	0.119
Smoking: Yes	20.278	<0.001	0.982
No	20.242		
Drinking alcohol: Yes	20.259	<0.001	0.703
No	20.958		
Use of a mobile phone: Yes	19.581	0.002	0.408
No	20.340		
Cumulative exposure amount of music	-0.052	0.014	0.038
GST antioxidation capability			
poor	19.906	0.002	0.494
normal	20.383		

Table 3. Univariate regression analysis of DPOAE amplitude levels for high frequencies (OAE_H3)

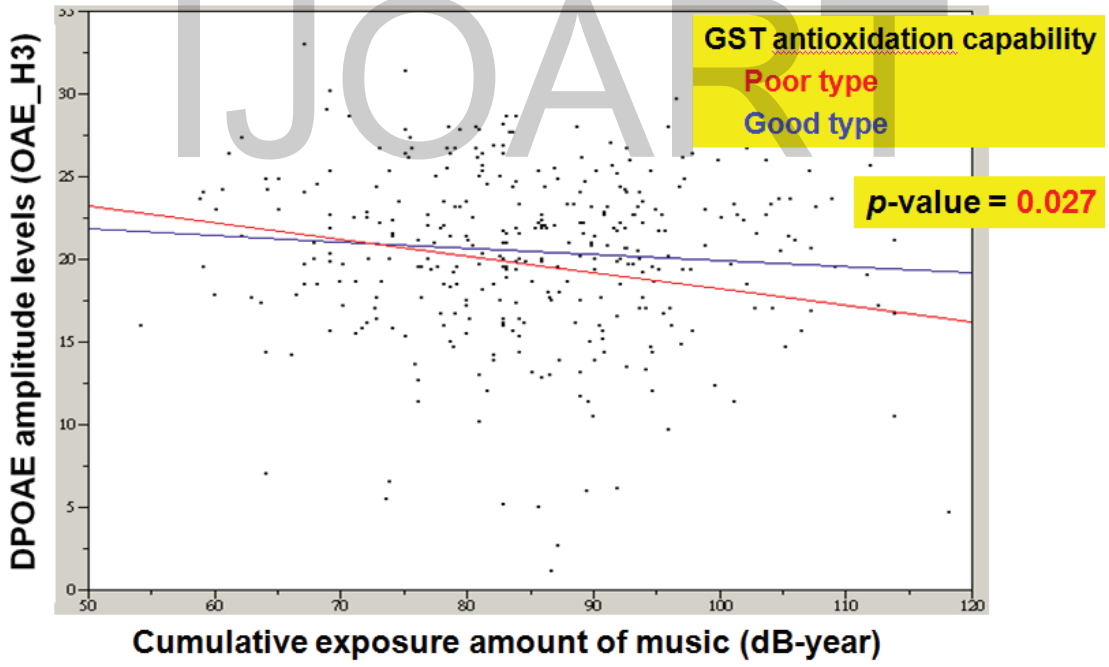

Figure 2. Relationship of cumulative exposure amount of music and DPOAE amplitude levels (OAE_H3)