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Effect of Smoking on Contralateral Suppression of Distortion Product Oto Acoustic Emissions (DPOAEs)

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ABSTRACT

The present study compared the contralateral suppression and the amplitude of distortion product otoacoutsic emissions (DPOAEs) between smokers and non-smokers to determine the influence of smoking. Thirty smokers and thirty non-smokers within the age range of 18-40 years with a normal hearing sensitivity were considered for the study. For both the groups, DPOAEs were measured and the efferent auditory system functioning was measured by presenting the white noise of 50 dB HL to the contralateral side, while recording the DPOAEs. There was no significant effect of age on the amplitude of DPOAEs in both the groups. However, there were significant differences in the amplitude of DPOAEs between smokers and non-smokers. The amount of suppression and DPOAE amplitude were reduced in smokers when compared to non-smokers. The study found no significant correlation between the amount of smoking and amount of suppression between smokers and non-smokers. However, there were significant correlations between the amount of smoking and DPOAE at low and mid frequencies between smokers and non-smokers. Therefore, the present study highlights the increased damage to the efferent auditory system risk and the smoking ill-effects on the efferent auditory system.

KEYWORDS

Smoking, DPOAE, Contralateral Suppression, OAE, DPOAE Amplitude

INTRODUCTION

Cigarette smoking is considered to be the dangerous public health threats with many adverse effects on the regular smokers (Ranson, 2002). According to the study by Room et al., (2005), smoking is associated with around 60 or more different medical conditions. Evidence has shown that smoking is responsible for many different illness and health issues, including cardiovascular diseases, circulation issues, cancers, respiratory diseases, stroke, vision loss and hair loss. As a result, smoking related issues itself currently costs the NHS of around £3.3bn per year (Scarborough et al., 2011).

Agarwal et al. (2008) stated that hearing loss is related to some common modifiable risk factors such as noise exposure, exercise (Hull and Kerschen 2010), cardiovascular

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disease (Gates et al. 1993) and diabetes (Horikawa et al. 2013). Cigarette smoking is considered to be the additional risk that is modifiable with the opportunities presented in the delaying severity of hearing loss.

Cigarette contains many toxic and dangerous ingredients, such as arsenic, mercury and nicotine which causes demyelination of nerves of the auditory pathway and can damage the outer hair cells (Cruickshanks et al. 1998). There have been several studies on how smoking affects threshold elevations, auditory system with abnormal otoacoustic emissions (OAEs) and absent auditory evoked potentials (Jedrzejczak 2015; Negley 2007; Giard 1994). Uchida. (2005) observed that excessive smoking causes damage to the outer hair cells (OHCs) and thus results in hearing loss. The PTA results showed that the deterioration of hearing at 4k Hz without noise exposure in smokers. Moreover, the effect of smoking on hearing loss with a dose-response was found at the frequencies of 500 Hz, 1k Hz and 2k Hz in middle-aged smokers. However, the participants included in this study were the smokers who had hearing loss that may be due to the outer hair cells (OHCs) damage.

Otoacoustic Emissions (OAEs) are considered as a sensitive and reliable measurement to detect the outer hair cells (OHC) function in the cochlea. Distortion product otoacoustic emission (DPOAE) is one type of OAEs recorded during the activation of cochlea. The measures of DPOAEs are by products of non-linear and normal behaviours resulting in the pre-neural status of the auditory system (Martin et al., 1990; Gorga et al., 1993, 1997, 2000). DPOAEs are recognised as an indicator of functioning of the cochlea because of its simple, quick, objective non-invasive and a certain level of frequency specificity (Brownell, 1990).

Furthermore, OAEs can be used to assess the function of the efferent system by contralateral suppression of OAEs. There is clear evidence that the stimulation of the auditory sound presented ipsilaterally or contralaterally, results in the amplitude reduction of both type of OAEs (TEOAEs and DPOAEs) (Moulin et al., 1993; Ryan et al., 1991; Collet et al., 1990). This is referred as the suppression of OAEs and also proved to be mediated through the medial efferent system (Williams et al., 1994; Kujawa et al., 1993; Veuillet et al., 1991).

Evidence has shown that the contralateral suppression of DPOAE is the decrease in the amplitude of about 1-4dB in the presence of contralateral acoustic stimulus (Chery-Croze et al; 1993). The study concluded that the frequency dependent is the suppression for at least the middle frequencies of 1 and 2 kHz. The DP-gram amplitude is altered by the contralateral acoustic stimulation (Durante, 2008).

Vinay. (2010) stated the age effect on the suppression of transient evoked otoacoustic emissions (TEOAEs) in smokers. The study reported the smoking effect on the contralateral suppression of TEOAEs was more in young adults. The results showed that there was no significant effect of age and effect of smoking on TEOAE amplitude

in smokers. However, there was a significant effect of age on the suppression amplitude of smokers. To the best of our knowledge, there are no studies that determined the contralateral suppression of distortion product otoacoustic emissions (DPOAEs) between smokers and non-smokers.

AIM OF THE STUDY

The main aim of this study was to investigate the effect of smoking on contralateral suppression of DPOAE. It was an attempt to determine the contralateral suppression differences across frequencies of DPOAE and correlation between smokers and non-smokers.

OBJECTIVES OF THE STUDY

- ✓ To assess the following:
  - Baseline distortion product otoacoustic emissions in both the groups i.e, control group (non-smokers) and the experimental group (smokers).
  - Contralateral suppression effects on distortion product otoacoustic emissions in both the groups (Smokers and non-smokers).
  - Comparing the mean amount of suppression values across frequencies between the two groups.
  - Comparing the mean amount of suppression values across frequencies between the two groups with ear specific (Right Ear and Left Ear).
  - Correlation between the following:
    - ➢ Overall suppression vs Overall DPOAE in smokers and non-smokers.
    - ➢ Amount of suppression vs DPOAE across each frequency in smokers and non-smokers.
    - ➢ Amount of smoking and suppression effects across individual frequencies and overall.

Therefore, the significant outcomes will show the risk of efferent auditory damage due to smoking and helps to develop awareness about the ill-effects of smoking on people's hearing and their nervous system.

METHODOLOGY

This is a quantitative experimental study design, consists of data collection, conducting test and data analysis.

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Participants

A total of 60 male participants who were in the age range of 18-40 years old were recruited. Of these, two groups were set up i.e, the control group of 30 participants who never smoked in their life. Another was the experimental group of thirty participants who had a history of smoking of 1 year minimum and are continuing to smoke with duration of 1-5 years. The number of cigarettes per day ranged from 4 to a pack with a frequency ranging from every day to once in a week. The participants with normal middle ear functioning and with no significant middle ear pathology, otological history and central nervous system disorders were included in the study. All the participants had hearing thresholds less than 25dBHL from 250 Hz to 8kHz and the participants with conductive and congenital hearing loss were excluded.

PROCEDURE

Complete case history of each subject was taken. They were asked to answer few general questions related to their smoking history (Appendix. II). Case history includes all the demographic data, otological history and the complete medical history.

Otoscopic Examination

Before the audiological testing, otoscopic examination was carried out. It is very important in identifying any ear wax, ear discharge or other middle ear conditions along with the condition of the tympanic membrane.

Pure tone audiometry

The suitable participants based on the inclusion criteria were invited to join the research. The researcher will explain the aim and the procedure to the potential participants. Once the participants read the information sheet and consent form and sign it, this means that they agreed to participate in this study (Appendix. III). Before starting the test, the participants were asked few general questions regarding their otological and smoking history (Appendix. II), followed by, the participant's hearing was examined through pure tone audiometry using the instrument that is calibrated (Siemens SD-270) and a pure tone average was calculated using the method of Hughson-Westlake. The audiometric thresholds of the participants which did not meet the inclusion criteria i.e, >25dBHL from 250 Hz to 8kHz were referred to the nearest clinic with a reference letter stating the query of hearing loss.

Tympanometry

To rule out middle ear pathology, tympanometry was carried out using r26 Resonance middle ear analyser. Static compliance values were taken by inserting probe tip in the

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ear canal. All the participants with normal middle ear status i.e, indicated by A type tympanogram.

DPOAE measurement

Distortion product otoacoustic emissions (DPOAEs) were done in all the participants using the Neurosoft Diagnostic Otoacoustic emissions (Neuro-Audio, version 2010). DPOAE was measured for the pure tone signals f1 and f2 at the ratio of 1.20 f2/f1. The intensity level was at 65 dB HL and 55 dB HL respectively. An overall signal to noise ratio of more than 6 dB SPL at all frequencies was considered as the presence of DPOAE.

CS-DPOAE measurement

Contralateral suppression of DPOAEs was done in all the subjects using the Neurosoft Diagnostic Otoacoustic emissions (Neuro-Audio). During DPOAE recording the white noise was presented at 50 dB SPL using insert ear phone to the subject's opposite ear. The amplitude of DPOAE with noise will be subtracted from DPOAE amplitude without noise to determine the amount of suppression.

DATA ANALYSIS

The normality test of Shapiro-Wilks was done to determine the normal distribution of the data. The data was not normally distributed as the histograms did not show bell-shaped curve. Therefore, non-parametric tests were administered. Wilcox sign rank test and Spearman's rank correlation was administered considering DPOAE and amount of suppression across different frequencies.

ETHICAL CONSIDERATION

Ethical application with the Project Reference Number PGT-1675 was awarded by Cardiff School of Sport and Health Sciences under the Cardiff Metropolitan University Ethics Framework.

RESULTS

Demographic data in three categories for smokers and non-smokers is illustrated in Table 1. The age range for non-smokers and smokers groups was from 18-35 and 19 to 47, respectively. Using chi-square test showed in the below table, between 18 to 25 (50%) of the respondents participated in the research from both the groups and there was no significant difference in the distribution of the age categories between smokers and non-smokers group (x^2=2.16, df=2; p>0.05).

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Table 1: Comparison of Demographic data in three age bands between non-smokers and smokers groups

AGE	NON-SMOKERS	SMOKERS
18-25	15	15
26-30	14	11
31 and above	1	4
Age of respondent	30	30

The PTA results for the non-smokers (11.5±3.6) and smokers (12.1±4.6) group ranged from normal (-10 dB to 15 dB) to minimal hearing level (16 dB to 25 dB) and the statistical results with respect to the hearing thresholds for both the groups are illustrated in Table 2.

Mann-Whitney U test was performed to compare the hearing thresholds between smokers and non-smokers. There were no significant statistical difference in the hearing thresholds in right ear, left and both ears between smokers and non-smokers group (Right ear: $U=824.10$, $p>0.05$; Left ear: $U=1266.00$, $p>0.05$; Both ears: $U=1744.500$, $p>0.05$).

Table 2: Comparison of PTA results averaged across frequencies of 500, 1k and 2k between non-smokers and smokers groups.

	Non-Smoker (M+/-SD)	Smoker (M+/-SD)
Right ear	11.32±3.38	12.0±4.82
Left ear	11.76±3.96	12.27±4.41
Both ears	11.54±3.65	12.14±4.58

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- **To assess baseline distortion product otoacoustic emissions in both the groups i.e, control group (non-smokers) and the experimental group (smokers).**

The baseline DPOAE was done in all the participants and the amplitude was recorded from 1 KHz to 8 KHz. Table 3 shows the mean DPOAE amplitudes and standard deviations in the right ears, left ears and both the ears in smokers and non-smokers groups.

Table 3: Comparison of Overall DPOAE across frequencies between non-smokers and smokers groups

	DPOAE in Right Ear (Mean+/-SD)	DPOAE in Left Ear (Mean+/-SD)	DPOAE of Both Ears (Mean+/-SD)
Non-smoker group	6.08/3.13	6.69/2.85	6.38/2.98
Smoker group	3.25/4.09	2.16/3.67	2.71/3.89

Because the amplitude of the DPOAE data between non-smokers and smokers were not normally distributed using Shapiro-Wilks test. Non-parametric test named Mann-Whitney (U) test was performed to compare the DPOAE amplitude between smokers and non-smokers. There was a significant statistical difference in overall DPOAE amplitude results between the smokers and non-smokers group ($U=864.500$, $p<0.05$). Furthermore, there were significant differences in the right ear and left ear DPOAE amplitude results between smokers and non-smokers ($U_{right}=269.500$, $p=.008$; $U_{left=}159.000$, $p<0.05$). Further analysis was conducted to compare the DPOAE amplitudes across frequencies of their right ears and left ears between smokers and non-smokers (Figures 1 & 2).

Figure 1: Comparing mean values of DPOAE at individual frequencies of right ear between non-smokers and smokers

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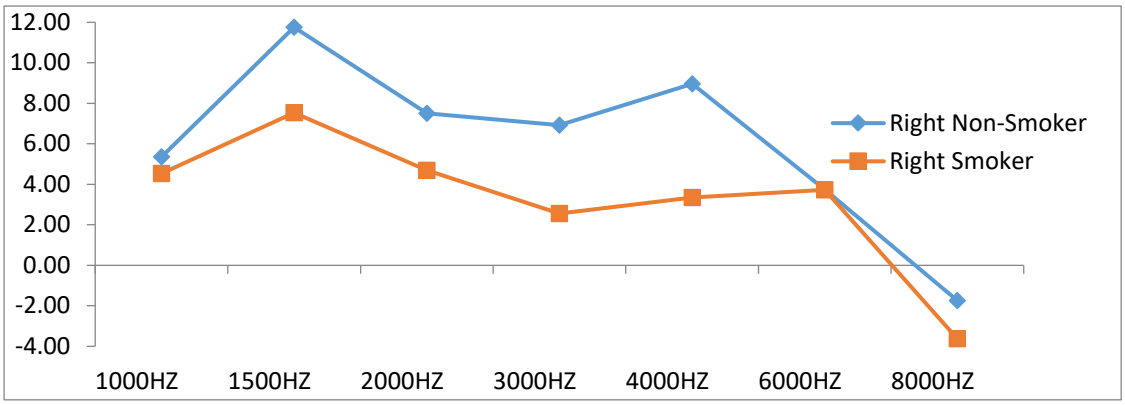
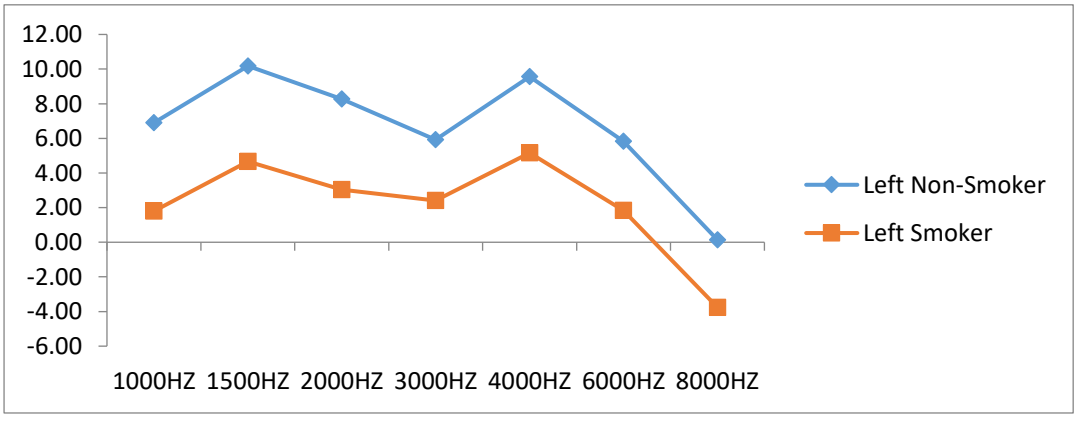


As shown in the Figure 1. The mean DPOAE amplitude values for the right ear at individual frequencies of smokers are 4.54, 7.53, 4.70, 2.56, 3.35, 3.73 and -3.63. Whereas, the mean DPOAE amplitude values of non-smokers are 5.36, 11.76, 7.51, 6.93, 8.97, 3.75 and -1.74 respectively.

Mann-Whitney descriptive statistics was performed to compare the right ear DPOAE amplitude across each frequency between non-smokers and smokers. There were significant differences in the DPOAE of the right ear at the mid frequencies of 1500 Hz, 3k Hz and 4k Hz ($p<0.05$) between non-smokers and smokers. In contrast, there were no significant differences in the DPOAE results at the low and high frequencies of 1k Hz, 2k Hz, 6k Hz and 8k Hz ($p>0.05$) between non-smokers and smokers.

Figure 2: Comparing mean values of DPOAE at individual frequencies of left ear between non-smokers and smokers



The mean DPOAE amplitude values for the left ear at individual frequencies of smokers are 1.79, 4.67, 3.04, 2.41, 5.16, 1.83 and -3.76. Whereas, the mean DPOAE amplitude

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values of non-smokers are 6.90, 10.18, 8.27, 5.93, 9.56, 5.83 and .14 respectively are shown in the Figure 2.

Mann-Whitney descriptive statistics was performed to compare the left ear DPOAE amplitude across each frequency between non-smokers and smokers. There were significant differences in the DPOAE results between non-smokers and smokers at each frequency ($p<0.05$).

- **To assess baseline contralateral distortion product otoacoustic emissions in both the groups i.e, control group (non-smokers) and the experimental group (smokers).**

Baseline CS-DPOAE was also done in all the participants by presenting noise in the opposite ear through insert earphones and the data was tabulated. Mean and standard deviation was calculated along with the individual frequencies as shown in Table 4, Figures 3 & 4 respectively.

Table 4: Comparing the Overall CSDPOAE between non-smokers and smokers groups

	CS-DPOAE in Right Ear (Mean+/-SD)	CS-DPOAE in Left Ear (Mean+/-SD)	CS-DPOAE of Both Ears (Mean+/-SD)
Non-smoker group	3.06/2.75	3.02/2.65	3.04/2.68
Smoker group	1.54/3.92	1.09/3.34	1.32/3.62

Further, the amplitude of the CS-DPOAE data between non-smokers and smokers were also not normally distributed using Shapiro-Wilks test. Non-parametric test named Mann-Whitney (U) test was performed to compare the CS-DPOAE amplitude between smokers and non-smokers. A significant statistical difference in overall CS-DPOAE amplitude and the left ear CS-DPOAE amplitude results was observed between the smokers and non-smokers ($U=1266.00$, $p<0.05$; $U_{left}=159.00$, $p<0.05$). Alternatively,

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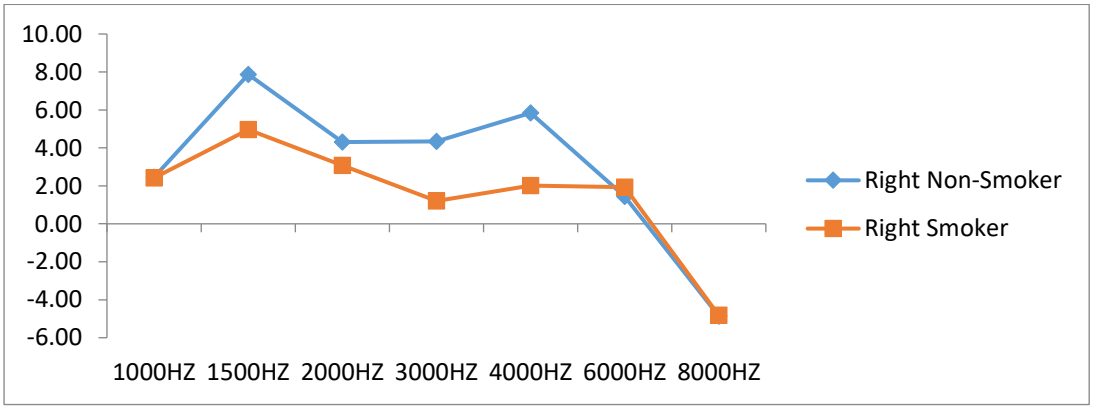
there was no significant difference in the right ear CS-DPOAE amplitude results between smokers and non-smokers (U_{right}=347.500, p>0.05).

The analysis was further carried out to compare CS-DPOAE amplitudes across frequencies of their right ears and left ears between smokers and non-smokers (Figures 3 & 4).

Figure 3: Comparing CSDPOAE at individual frequencies of right ear between smokers and non-smokers groups



As shown in the Figure 3. The mean CS-DPOAE amplitude values for the right ear at individual frequencies for smokers are 2.42, 4.96, 3.08, 1.21, 2.01, 1.93 and -4.82. Whereas, the mean CS-DPOAE amplitude values of non-smokers are 2.45, 7.87, 4.31, 4.35, 5.85, 1.44 and -4.86.

The descriptive statistics of Mann-Whitney was performed to compare the right ear CS-DPOAE amplitude across each frequency between non-smokers and smokers. The significant differences in the CS-DPOAE of the right ear at the mid frequencies and high frequencies of 1500 Hz, 3k Hz and 4k Hz (p<0.05) was observed between non-smokers and smokers. In contrast, there were no significant differences in the CS-DPOAE results at the low and high frequencies of 1k Hz, 2k Hz and 6k Hz (p>0.05) between non-smokers and smokers.

Figure 4: Comparing the average CSDPOAE at individual frequencies of left ear between smokers and non-smokers groups

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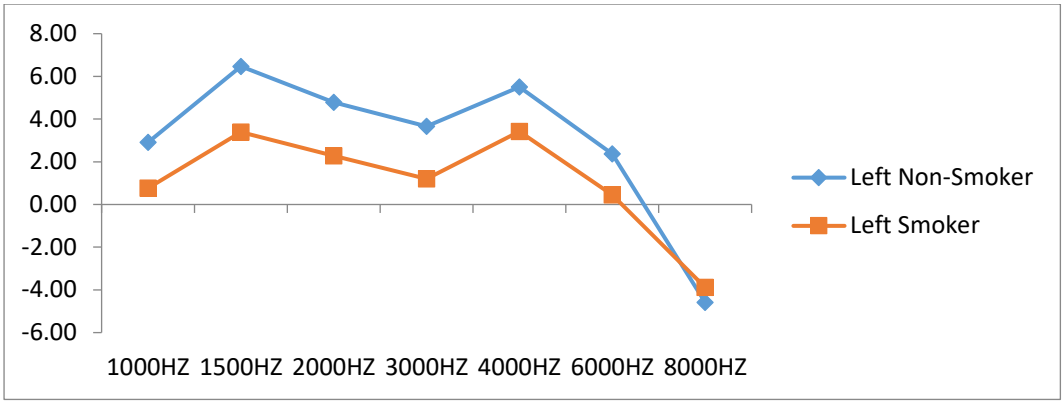

As shown in the figure 4. The mean CS-DPOAE amplitude values for the left ear at individual frequencies of smokers are .77, 3.40, 2.29, 1.20, 3.42, .45 and -3.88. Whereas, the mean CS-DPOAE amplitude values of non-smokers are 2.91, 6.47, 4.78, 3.66, 5.51, 2.36 and -4.59 respectively.

Mann-Whitney descriptive statistics was performed to compare the right ear CS-DPOAE amplitude across each frequency between non-smokers and smokers.

There were significant differences in the CS-DPOAE of the left ear at the mid and high frequencies of 1500 Hz, 2k Hz and 3k Hz ($p<0.05$) between non-smokers and smokers. In contrast, there were no significant differences in the CS-DPOAE results at the low and high frequencies of 1k Hz, 4k Hz, 6k Hz and 8k Hz ($p>0.05$) between non-smokers and smokers.

- **To assess the comparison of the mean amount of suppression values across frequencies between both the groups i.e, control group (non-smokers) and the experimental group (smokers).**

The suppression amount was determined in the study by the DPOAE amplitude subtraction with noise from the amplitude of DPOAE without noise. The mean and standard deviation of the amount of suppression in both smokers and non-smokers for the left, right and both the ears is given in Table 5.

Table 5: Comparing overall suppression effects between smokers and non-smokers groups

	AOS in Right Ear (Mean+/-SD)	AOS in Left Ear (Mean+/-SD)	AOS of Both Ears (Mean+/-SD)
Non-smoker group	3.03/.88	3.56/1.46	3.30/1.22

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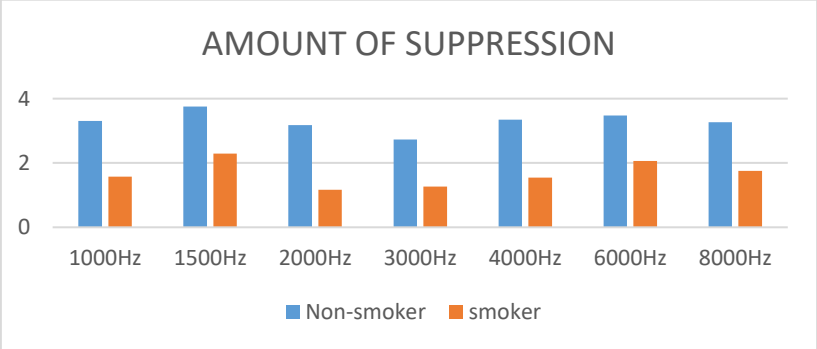
Smoker group	1.83/.70	1.51/.70	1.67/.71

Descriptive analysis was performed using Mann-Whitney (U) to compare the amount of suppression between smokers and non-smokers groups. The test results were 322.00, ($p=0.000$; $p<0.05$). Therefore, there is significant statistical difference between smokers and non-smokers overall amount of suppression across frequencies. Furthermore, the amount of suppression of right ear results between non-smokers and smokers is 123.000, ($p<0.0005$) and the left ear Mann-Whitney (U) results is 49.000, ($p<0.0005$). Therefore, there is significant difference between the right ear and left ear amount of suppression between smokers and non-smokers.

Figure 5: Comparing the mean amount of suppression across frequencies between smokers and non-smokers groups



As shown in the figure 5. The mean values of the amount of suppression across different frequencies for smokers are 1.58, 2.29, 1.17, 1.27, 1.55, 2.06 and 1.75. Whereas, the mean values of the amount of suppression across frequencies for non-smokers are 3.31, 3.75, 3.18, 2.73, 3.35, 3.48 and 3.27 respectively.

Mann-Whitney descriptive statistics was performed to compare the overall amount of suppression across each frequency between non-smokers and smokers groups. There is significant difference in the results between non-smokers and smokers at all the frequencies, where ($p<0.05$). The overall results showed the reduced amount of suppression in smokers when compared with non-smokers indicating efferent auditory system dysfunction.

- **To assess the correlation of Overall suppression vs Overall DPOAE between both the groups i.e, control group (non-smokers) and the experimental group (smokers)**

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Spearman's rank correlation was conducted DPOAE amplitudes and amount of suppression. Overall suppression vs overall DPOAE results in both smokers and non-smokers were shown in Table 6.

Table 6: Overall suppression vs Overall DPOAE results in both smokers and non-smokers

Overall suppression effects and overall DP (R, L and both)		Correlation	P
Non-Smoker	Right	.432*	.017
	Left	.340	.066
	Both	.375**	.003
Smoker	Right	.324	.080
	Left	.077	.688
	Both	.195	.135

For non-smokers, the significant correlations between overall suppression and overall DPOAE were found in right ear ($r=0.432$, $p<0.05$), (left ear=0.340, $p<0.05$) and (both ears=0.375, $p<0.05$). For smokers, there were no significant correlations between the amount of suppression and DPOAE in the right ear, left ear and both the ears (right ear = 0.324, $p>0.05$); (left ear=0.077, $p>0.05$); and (both ears=0.195, $p>0.05$).

- **To assess the amount of suppression vs DPOAE across each frequency between both the groups i.e, control group (non-smokers) and the experimental group (Smokers).**

Significant correlations were found between the amount of suppression and DPOAE at the frequencies of 1k Hz, 1500 Hz, 2k Hz, 3k Hz, 4k Hz and 6k Hz of DPOAE and 1500

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Hz, 3k Hz and 4k Hz of amount of suppression but no significance at other frequencies in non-smokers group. In contrast, significant correlations were found between the amount of suppression and DPOAE at the frequencies of 1k Hz, 1500 Hz and 2k Hz respectively but no significance ($p>0.05$) at other frequencies in smokers group as shown in the Tables 6 & 7 respectively.

Table 7: Correlations of amount of suppression vs DPOAE across each frequency in non-smokers group

DPOAE	Sup_ 1kHz	Sup_1 500Hz	Sup_ 2kHz	Sup_3 kHz	Sup_4 kHz	Sup_ 6kHz	Sup_8 kHz
1kHz	-.035	-.0.67	.161	.208	.104	.295*	-.162
1500Hz	.078	.438**	.208	.064	-.066	.026	-.162
2kHz	.136	.355**	.329*	.166	-.038	.086	-.163
3kHz	.006	.242	.097	.109	.408**	-.007	-.152
4kHz	.024	.242	.197	.175	.455**	-.103	-.003
6kHz	.066	.281*	.234	.369**	.374**	.397*	-.006
8kHz	.142	.011	.294*	.220	.046	.151	.109

From the above table, the correlations were significant at the level of 0.05.

Table 8: Correlation of DPOAE and amount of suppression across each frequency in smokers group

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DPOAE	Sup_1 kHz	Sup_1 500Hz	Sup_2 kHz	Sup_3 kHz	Sup_ 4kHz	Sup_6 kHz	Sup_8 kHz
1kHz	.326**	.336**	.337**	-.153	.103	.006	-.048
1500Hz	.349**	.456**	.308*	-.095	.074	.135	.130
2kHz	.283**	.459**	.416**	.069	.225	.047	.127
3kHz	.212	.161	.144	-.042	.192	.146	-.251
l4kHz	-.043	.028	-.010	-.053	.020	-.008	-.412**
6kHz	.288*	.213	-.047	-.063	.184	.116	-.281*
8kHz	.080	.166	.015	-.088	-.000	.040	-.135

From the above table, the correlations were significant at the level of 0.05.

- **To assess the correlation of amount of smoking and suppression effect between both the groups i.e, control group (non-smokers) and the experimental group (Smokers).**

The spearman's correlation determined a significance level of 0.05 between the amount of smoking and suppression. No significant statistical differences between the amount of suppression to the amount of smoking across all the frequencies and the overall amount of suppression and the amount of smoking ($p>0.05$). In contrast, there were significant statistical differences between the overall DPOAE and the amount of smoking across all frequencies ($p<0.05$). The amount of smoking and the baseline DPOAE at the low and mid frequencies of 1k Hz, 1500 Hz, 2k Hz and 3k Hz ($p<0.05$) differed significantly, alternatively, there were no significant differences in the amount of smoking and the baseline DPOAE at the high frequencies of 4k Hz, 6k Hz and 8k Hz ($p>0.05$).

DISCUSSION

The interference of cigarette smoking to the tasks done by the outer hair cells leads to the dysfunction of the cochlea and affecting the hearing thresholds especially in the higher frequencies within the frequency range of 250-8000 Hz. The findings obtained

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from the present study showed that the mean values of DPOAE amplitude at all frequencies of the both right ear and left ear of non-smokers were higher than smokers group. And also the amplitude values were less at higher frequencies when compared to lower frequencies.

Negley. (2007) found a reduction in DPOAEs in the frequency range of 2-8 kHz in smokers when compared to non-smokers because of the correlation between the outer hair cells and OAEs, the metabolic cochlear disruption impacting the DPOAEs and poorer thresholds point out the dysfunction of cochlea. Whereas, Torre et al. (2007) in the group study with the frequency range that is similar determined with a less use of cigarette, there were levels of reduction observed. However, both studies did not compare the DPOAE reduction in the frequencies below 2k Hz.

Recent research related to occupational noise exposure also evaluated the joint effects of smoking, noise exposure, age and ototoxicity on hearing loss (Siegelaub et al., 1974; Barone et al., 1987; Virokannas and Anttonen, 1995; Starck et al., 1999; Toppila et al., 2001; Mizoue et al., 2003; Nomura et al., 2005; Uchida et al., 2005). The results of the study showed that the smoking, age, noise-exposure and ototoxicity together produces the greater risk for the hearing loss than smoking, age, noise-exposure and ototoxicity alone. Cigarette burning releases the organic solvents such as toluene, mercury, lead and carbon monoxide which causes synergism when interacted with noise causing NIHL. The pathogenic mechanisms established are the vascular changes such as the cochlear hypoxia, increased levels of blood viscosity and the capillary vasoconstriction, in relation to smoking and the noise exposure causing hearing loss and efferent system damage.

Moulin et al. (1990) stated that the contralateral broad-band noise (BBN) has a suppression effect on the recorded DPOAE from the frequencies 1k Hz to 4k Hz. This effect was not because headphones and their cross-hearing nor because of the noise floor without a change in increasing the contralateral stimulation. Deter et al. (2005) studied the stimulation of contralateral suppression in the noise levels 60, 70 and 80 dB SPL in adults, reduced DPOAEs amplitude and the effects of suppression with increased noise levels. From the findings of the present study, the mean values of CS-DPOAE amplitude at all frequencies of right ear showed higher values in non-smokers when compared to smokers, except at the frequency of 6k Hz and 8k Hz. Whereas, the left ear CS-DPOAE mean values of non-smokers were higher than the smokers at all frequencies except at the frequency of 8k Hz. Moreover, the average amount of suppression values at each frequency was higher in non-smokers when compared to smokers, indicating reduced amount of suppression in smokers when compared to non-smokers. These results are in keeping with the findings reported by Prabhu. (2017). In this study, the authors reported that the amount of suppression was reduced significantly in smokers when compared to non-smokers, and thus they suggested the efferent auditory system dysfunction in smokers. The outer hair cells

receive the innervations rich in the efferent systems from the central nervous system and the OAE changes with the stimulation externally reflecting the CNS influence on the activity of outer hair cells.

Howard et al. (1998) reported that the atherosclerotic damage was more smokers susceptible and also reported the cigarettes number increases and the number of years smoked increases the atherosclerotic damage because of the oxygen deprivation of the hair cells and the spiral ganglion. The tobacco free radicals such as the arsenic and mercury damage the hair cells affecting the neurotransmitters release (Cruickshanks, 1998), influencing the functioning of the efferent system. The abnormal measurement results of auditory evoked potentials are seen in smokers with respect to the damage in the afferent auditory system (Gupta, 2008). There are no specific studies affecting the efferent auditory nervous system, anatomic abundance suggests that the efferent system involves several disorders, but only little evidence on supporting the hypotheses as the bundles of the cochlear efferent system travels with the vestibular nerve central portion (Scharf, 1997).

Cigarette smoking has an association with hearing loss because of the mechanisms that are anti-oxidative or vascular supply to the auditory system. Weiss. (1970) found that the men with history of smoking more than a pack per day had the hearing thresholds worsen at the frequencies from 250 Hz to 1k Hz when compared to non-smokers, but no difference at the higher frequencies. The findings also reported an association with the environmental exposure of tobacco smoke in the home with the effects of passive smoking on the sensitivity of hearing in children.

In this study, there was no significant correlation between the amount of suppression and number of cigarettes. The length of smoking and the number of pack (5-6yrs) was relatively small in this study. The smoking effect is seen very clearly especially in people who smoke 30-40 pack-years (Cruickshanks, 1998). Passive smoking affects the mediators of the biological cardiovascular diseases including the changes in the activation of platelets and the cell dysfunction of endothelial. Barnoya. (2006) examined the nicotine dependency in smokers and non-smokers and found that passive smokers were triggered with the receptors of nicotine and also were susceptible for lower respiratory tract diseases (Benowitz, 2009), breast cancer, head and neck cancer and vascular diseases (Rubinstein, 2009). However, the study results could not explain the relation between the amount and length of smoking with hearing loss, suggesting for future research.

CONCLUSION

The results of this study showed the significant difference in the amount of suppression, DPOAE amplitude (overall, right and left ear) and CS-DPOAE (overall and left ear) between smokers and non-smokers. However, there were no significant differences in the contralateral suppression of DPOAE amplitude right ear results between smokers and non-smokers.

Spearman's correlation determined significant correlations between the amount of smoking and DPOAE at the low and mid frequencies of 1k Hz, 1500 Hz, 2k Hz and 3k Hz, no significant statistical difference in the amount of smoking and DPOAE at high frequencies of 4k Hz, 6k Hz and 8k Hz and the amount of smoking and amount of suppression across all frequencies between smokers and non-smokers. Therefore, indicating efferent system damage and smoking effects on the auditory system. Ultimately, it can be mentioned that there needs to be more research done on the smoking effect on the efferent system with the better understanding of the mechanisms underlying.

REFERENCES

Attias, J., Bresloff, I., Reshef, I., Horowitz, G. and Furman, V., 1998. Evaluating Noise Induced Hearing Loss with Distortion Product Otoacoustic Emissions. *British Journal of Audiology*, 32(1), pp.39-46.

Attias J, e., 2020. *Detection And Clinical Diagnosis Of Noise-Induced Hearing Loss By Otoacoustic Emissions. - Pubmed - NCBI*. [online] Ncbi.nlm.nih.gov. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/12678938/> [Accessed 15 May 2020].

Andeol, G., Guillaume, A., Micheyl, C., Savel, S., Pellieux, L. and Moulin, A. (2019). Auditory Efferents Facilitate Sound Localization in Noise in Humans.

Berlin, C., Hood, L., Wen, H., Szabo, P., Cecola, R., Rigby, P. and Jackson, D. (1993). Contralateral suppression of non-linear click-evoked otoacoustic emissions. Hearing Research, 71(1-2), pp.1-11.

Carhart, R. and Jerger, J. (1959). Preferred Method For Clinical Determination Of Pure-Tone Thresholds. Journal of Speech and Hearing Disorders, 24(4), pp.330-345.

Chan, L. (2016). Effects of Cigarette Smoking in Adults. MacEwan University Student eJournal, 3(1).

Cruickshanks, K., Klein, R., Klein, B., Wiley, T., Nondahl, D. and Tweed, T. (1998). Cigarette Smoking and Hearing Loss. JAMA, 279(21), p.1715.

Dawes, P., Cruickshanks, K., Moore, D., Edmondson-Jones, M., McCormack, A., Fortnum, H. and Munro, K., 2014. Cigarette Smoking, Passive Smoking, Alcohol Consumption, and Hearing Loss. *Journal of the Association for Research in Otolaryngology*, 15(4), pp.663-674.

De Boer, J. and Thornton, A. (2008). Neural Correlates of Perceptual Learning in the Auditory Brainstem: Efferent Activity Predicts and Reflects Improvement at a Speech-in-Noise Discrimination Task. Journal of Neuroscience, 28(19), pp.4929-4937.

Giard, M., Collet, L., Bouchet, P. and Pernier, J. (1994). Auditory selective attention in the human cochlea. Brain Research, 633(1-2), pp.353-356.

Gopal, K., Herrington, R. and Pearce, J. (2009). Analysis of Auditory Measures in Normal Hearing Young Male Adult Cigarette Smokers Using Multiple Variable Selection Methods with Predictive Validation Assessments. International Journal of Otolaryngology, 2009, pp.1-7.

Gupta, P., Sood, S., Atreja, A. and Agarwal, D. (2008). Evaluation of brain stem auditory evoked potentials in stable patients with chronic obstructive pulmonary disease. Annals of Thoracic Medicine, 3(4), p.128.

Harrison, W. and Norton, S. (1999). Characteristics of Transient Evoked Otoacoustic Emissions in Normal-Hearing and Hearing-Impaired Children. Ear and Hearing, 20(1), pp.75-86.

Howard, G. (1998). Cigarette Smoking and Progression of Atherosclerosis. JAMA, 279(2), p.119.

Jedrzejczak, W., Koziel, M., Kochanek, K. and Skarzynski, H. (2015). Otoacoustic Emissions in Smoking and Nonsmoking Young Adults. Clinical and Experimental Otorhinolaryngology, 8(4), p.303.

Jha, P., Ranson, M., Nguyen, S. and Yach, D. (2002). Estimates of Global and Regional Smoking Prevalence in 1995, by Age and Sex. American Journal of Public Health, 92(6), pp.1002-1006.

Khalfa, S., Bougeard, R., Morand, N., Veuillet, E., Isnard, J., Guenot, M., Ryvlin, P., Fischer, C. and Collet, L. (2001). Evidence of peripheral auditory activity modulation by the auditory cortex in humans. Neuroscience, 104(2), pp.347-358.

Kumar, U. and Vanaja, C. (2004). Functioning of Olivocochlear Bundle and Speech Perception in Noise. Ear and Hearing, 25(2), pp.142-146.

Lisowska, G., Namyslowski, G., Orecka, B. and Misiolek, M. (2019). Influence of aging on medial olivocochlear system function.

Lowe, G., Drummond, M., Forbes, C. and Barbenel, J. (1980). The Effects of Age and Cigarette-Smoking on Blood and Plasma Viscosity in Men. Scottish Medical Journal, 25(1), pp.13-17.

Mostaghaci, M., Mehrparvar, A., Mollasadeghi, A., Hashemi, S., Sakhvidi, M. and Davari, M. (2015). Simultaneous effects of noise exposure and smoking on OAEs. Noise and Health, 17(77), p.233.

Munjal, S. (2017). Effect of Chronic Tobacco Smoking on Hearing among Men. Global Journal of Otolaryngology, 7(4).

Negley, C., Katbamna, B., Crumpton, T. and Lawson, G. (2007). Effects of Cigarette Smoking on Distortion Product Otoacoustic Emissions. Journal of the American Academy of Audiology, 18(8), pp.665-674.

Reavis, K., Phillips, D., Fausti, S., Gordon, J., Helt, W., Wilmington, D., Bratt, G. and Konrad-Martin, D., 2008. Factors Affecting Sensitivity of Distortion-Product Otoacoustic Emissions to Ototoxic Hearing Loss. *Ear and Hearing*, 29(6), pp.875-893.

Reiter, E. and Liberman, M. (1995). Efferent-mediated protection from acoustic overexposure: relation to slow effects of olivocochlear stimulation. Journal of Neurophysiology, 73(2), pp.506-514.

Rubinstein M, Hildesheimer M, Zohar S, Chilarovitz T. (1997). Chronic cardiovascular pathology and hearing loss in the aged. Gerontology 23:4-9.

Schane, R., Ling, P. and Glantz, S., 2010. Health Effects of Light and Intermittent Smoking. *Circulation*, 121(13), pp.1518-1522.

Uchida, Y., Nakashima, T., Ando, F., Niino, N. and Shimokata, H. (2005). Is there a relevant effect of noise and smoking on hearing? A population-based aging study International Journal of Audiology, 44(2), pp.86-91.

Vinay (2010). Effect of smoking on transient evoked otoacoustic emissions and contralateral suppression. Auris Nasus Larynx, 37(3), pp.299-302.

Wilson D, Parsons J, Wakefield M. (1999). The health related quality-of-life of never smokers, ex-smokers, and light, moderate, and heavy smokers. Prev Med, 29(3):139-144.

Zhao, F. and Stephens, D., 1996. Hearing complaints of patients with King-Kopetzky Syndrome (obscure auditory dysfunction). *British Journal of Audiology*, 30(6), pp.397-402.

APPENDIX 1: SUPPORTING LETTER

Shravya®
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To whom it may concern,

Kindly note that Shravya Speech and Hearing Center is in support of the research project "Effect of Smoking on Contralateral Suppression of Distortion Product Oto Acoustic Emissions".

This study was proposed by Ms. Sindhuja Nadella (Under Dr. Fei Zhao's supervision) a MSc Audiology student of Cardiff Metropolitan University.

This study aims to compare amplitude and suppression across frequencies in smokers and non-smokers.

We feel that the project is important and timely. As a result, we would like to help Ms. Sindhuja Nadella and provide support in order for her to complete her study.

Through this letter, we acknowledge specific roles and responsibilities we will fulfil in this partnership.

We look forward to working with Ms. Sindhuja Nadella

Shiva Prasad Boddupally
Chief Audiologist & Clinical Specialist in Cochlear Implants

Date: 6/09/2018

Shravya Speech & Hearing Center Hyderabad-38 S.R. Nagar

• Hearing Evaluation • Hearing Aid Trial & Fitting • Speech & Language Evaluation and Therapy
• Pre Cochlear Implant Assessment • Post Implant Mapping / Habilitation
• Hearing Aid / Cochlear Implant Accessories • Ear Moulds

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APPENDIX II: CASE HISTORY QUESTIONNAIRE

Ethics Reference Number:
Name of Researcher: Sindhuja Nadella
Name of Supervisor: Dr. Fei Zhao
Project title: Effect of smoking on contralateral suppression of Distortion Product Otoacoustic Emissions (DPOAE).

CASE HISTORY QUESTIONNAIRE

Name:

Age/Gender:

Phone number:

Address:

History of the Client:

Do you have smoking habit? Yes/No

If Yes, since when?

From how many years have you been smoking?

How many do you smoke per day?

How frequent do you smoke?

Do you have any breathing related problems? Yes/No

Do you have any history of hearing loss or do you have hearing loss at present? Yes/No

Do you have any history of ear discharge or earache? Yes/No

Do you have any history of middle ear infection? Yes/No

Do you work under noise environment? Yes/No

Do you have any physical trauma related to head? Yes/No

Do you have any other health issues? (TB, BP, Diabetes) Yes/No

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APPENDIX III: **PARTICIPANT INFORMATION SHEET**

Ethics reference number:
Title of Project : Effect of Smoking on Contralateral Suppression of Distortion Product Otoacoustic Emissions (DPOAE)

Student researcher: Sindhuja Nadella

Supervisor: Fei Zhao

Participant Information Sheet

Background

My name is Sindhuja Nadella, and I am MSc second year Audiology student at Cardiff Metropolitan University. I am currently carrying out my dissertation project under the supervision of Dr Fei Zhao. This project aims to explore the knowledge on the effect on smoking on the contralateral suppression of DPOAE (Distortion Product Oto Acoustic Emissions) by investigating the DPOAE amplitude and amount of suppression across frequencies among smokers and non-smokers.

Cigarette smoking is reported to be one of the most common health hazard reported in general population (Ranson,2002). There are several other studies reported in the literature suggesting that smoking can have adverse effects on the auditory system with elevation of threshold, abnormal otoacoustic emissions (OAE) and abnormal auditory evoked potentials (Jedrzejczak, 2015). The efferent auditory system also plays an important role in human auditory system which is generally assessed using contralateral suppression of otoacoustic emissions (OAE) where there is reduction of amplitude of OAE in the order of 1-4 dB due to a suppressor stimulus (Berlin, 1993). Therefore, the main aim of this study is to investigate the amplitude and amount of suppression across frequencies among smokers and non-smokers. Thus, the results will show how chronic smoking habits increases the risk of efferent auditory damage highlighting the ill-effects of smoking on efferent auditory system. This will help in developing more knowledge and awareness among people about the adverse effects of smoking on their hearing and their central, peripheral nervous system.

Your Participation in the research study

This study will include a small set of general questions to be answered before taking part in the hearing assessment which includes Pure tone audiometry (PTA), immitance audiometry, DPOAE and CS-DPOAE.

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Inclusion Criteria

1. You are within the age of 18-40 years old.
2. You have normal hearing with hearing thresholds less than 25 dBHL from 250 Hz to 8KHz.
3. You have a history of smoking ranging from 1 year-5 years and number of cigarettes per day ranging from 4/day to a pack/day and the frequency of smoking ranging from every day to once in a week or never smoked in your life.
4. You have no significant otological history, noise exposure, intake of ototoxic drugs, diabetes and no middle ear pathology or other central or peripheral nervous disorders.

Participation in this research is voluntary. You have the right to withdraw your information up to two weeks after your participation (i.e., completion of the audiological tests). If you decide to withdraw, all data will be destroyed and not used within the research.

If you choose to take part in this research you will be asked your convenient time and date within a given time period for the test to be conducted. The test is completely safe, non-invasive and a quick test which takes about 10 to 30 seconds for each ear and another 10-15 minutes for the overall test. Insert earphone, tiny probe is used which is neither harmful nor painful.

Consent

A consent form will be enclosed to the front of the study. The form must be completed before completing the Study. Please return the consent form before the study starts.

Are there any risks?

All tests carried out in this project are simple, quick and non-invasive. During the test, you will hear some soft sounds. If you feel uncomfortable, please feel free to let the researcher know and the study will be stopped immediately. There are no further risks of completing this study.

What will happen to the results of the study?

The results gained will help give insight among individuals about the effects of smoking on auditory system and also the central-peripheral nervous system. The results will also provide insight into attitudes of the people towards smoking and also audiologists which will help to identify areas for improvement of the people's betterment.

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If you wish to be de-briefed after the research project has been completed, this can be arranged at a later date via the contact details below.

Protecting your privacy:

All information gathered during the study will remain completely anonymous. After the research is completed all the data collected will be destroyed after the final exam board in July 2020. Your data will not be used for any other purpose aside from this study.

Further information

If you have any questions about the research please do not hesitate to contact my supervisor Dr Fei Zhao (E-mail: fzhao@cardiffmet.ac.uk).

Thank you for taking your time to read this information sheet and considering taking part in this research.

Sindhuja Nadella
Audiology postgraduate student
MSc Advanced Practice (Audiology)

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Appendix IV: PARTICIPANT CONSENT FORM
Reference Number:
Participant name or Study ID Number:
Student researcher: Sindhuja Nadella
Supervisor: Fei Zhao

Title of Project: EFFECT OF SMOKING ON CONTRALATERAL SUPRESSION OF DISTORTION PRODUCT OTOACOUSTIC EMISSIONS (DPOAE)

PARTICIPANT CONSENT FORM

Participant to complete this section: Please initial each box.

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time before leaving the experiment, without giving any reason. ☐
3. I agree to take part in the above study. ☐
4. I agree to the use of anonymised quotes in publications ☐

_____ _____

Signature of Participant Date

_____ _____

Name of person taking consent Date

_____

Signature of person taking consent

** When completed, 1 copy for participant & 1 copy for researcher site file*