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Sex-Related Cochlear Impairment in Cigarette Smokers

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: A number of studies have documented the influence of cigarette smoking on hearing. However, the association between sex and hearing impairment in smokers as measured by otoacoustic emissions (OAEs) has not been clearly established. The aim of this study was to analyze sex-specific effects of smoking on hearing via conventional and ultra-high-frequency pure tone audiometry (PTA), and OAEs, specifically spontaneous OAEs, click-evoked OAEs, and distortion-product OAEs.

Material/Methods: The study included 84 healthy volunteers aged 25–45 years (mean 34), among them 46 women (25 non-smokers and 21 smokers) and 38 men (16 non-smokers and 22 smokers). The protocol of the study included otoscopic examination, tympanometry, low-, moderate-, and ultra-high-frequency PTA, evaluation of spontaneous click-evoked (CEAOEs) and distortion-product otoacoustic emissions (DPOAEs), assessment of the DP-grams for $2f_1$-f_2 (f_1 from 977 to5 164 Hz), and input/output function at L_2 primary tone level of 40–70 dB SPL.

Results: Smokers and non-smokers did not differ significantly in terms of their hearing thresholds assessed with tone audiometry. Male smokers presented with significantly lower levels of CEAOEs and DPOAEs than both male non-smokers and female smokers.

Conclusions: Smoking does not modulate a hearing threshold determined with PTA at low, moderate, and ultra-high frequencies, but causes a significant decrease in OAE levels. This effect was observed only in males, which implies that they are more susceptible to smoking-induced hearing impairment. Sex-specific differences in otoacoustic emissions level may reflect influences of genetic, hormonal, behavioral, and/or environmental factors.

MeSH Keywords: Hearing Loss • Otoacoustic Emissions, Spontaneous • Smoking

Full-text PDF: http://www.medscimonit.com/abstract/index/idArt/899589

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Background

Our knowledge regarding the harmful effects of tobacco smoke on hearing is still limited. Smoking was shown to result in vascular lesions and changes in some characteristics of the blood, leading to hypoxia-induced injury of various tissues, including the organ of hearing [1–3]. Researchers from the University of Washington in Seattle (United States) and University of Melbourne (Australia) analyzed the 1980–2012 data on the prevalence of cigarette smoking in 187 countries. They showed that the number of smokers older than 15 years of age increased from 721 million in 1980 to roughly one billion (967 million) in 2012. Also, the total number of smoked cigarettes increased, from 4.96 billion to 6.25 billion annually. Currently, the population of male and female smokers is estimated at 31% and 6.2% worldwide, respectively; 30 years earlier, these were 41% and 10%, respectively. According to the WHO data from 2011, the number of adult smokers in Poland is 28% lower than in 1995. Nevertheless, 27.2% of adults in Poland smoke and mean cigarette consumption is 15.4 per day. The percentages of male and female smokers in Poland are estimated at 33.6% and 20.5% of the adult population, respectively. The vast majority of Polish smokers are individuals between 45 and 59 years of age (36%), with 62.5% having primary or vocational education and 43% currently unemployed [4].

Exposure to harmful components of cigarette smoke leads to disorders of lipid metabolism and vascular endothelial dysfunction, which is reflected by enhanced atherosclerosis and increase in blood viscosity [1,2,5,6]. Carbon oxide present in tobacco smoke is a substrate for carboxyhemoglobin synthesis. Despite markedly higher affinity than hemoglobin, carboxyhemoglobin delivers significantly less oxygen to the tissues [7–10]. The vasoconstrictive effect of nicotine results in an impairment of tissue perfusion, which may be associated with cellular dysfunction in the case of chronic exposure to tobacco smoke [1,2,5,9]. According to one hypothesis, the harmful effects of tobacco smoke on hearing are associated with the toxic dysfunction of nicotinic acetylcholine receptors (nAChRs), a vital component of the hearing pathway [11,12]. Moreover, the toxic components of cigarette smoke were shown to impair the redox system, which was reflected by enhanced tissue hypoxia and injury, inter alia impairment of the active mechanisms of the outer hair cells (OHCs) of the cochlea [13–15]. Measurement of OAEs is the only available non-invasive test for selective analysis of the OHC activity, enabling simple, objective, and highly sensitive functional examination of the hearing organ [16,17].

The aim of this study was to analyze the sex-specific effect of cigarette smoking on the results of subjective and objective examination of hearing, namely ultra-high frequency PTA, spontaneous otoacoustic emission (SOAE), and CEOAE and DPOAE levels.

Material and Methods

The study included 84 healthy volunteers aged between 25 and 45 years (mean 34 years), among them 41 non-smokers (mean age 33.3 years) and 43 smokers (mean age 34.7 years). The sample comprised 46 women (25 non-smokers and 21 smokers) and 38 men (16 non-smokers and 22 smokers). None of the participants had a history of audiological impairment. The group of smokers included the individuals who smoked at least 15 cigarettes per day for at least 7 years. The group of non-smokers included only the individuals who had never smoked. The exclusion criteria of the study were: abnormal result of otoscopic examination, history of ear problems, conductive hearing impairment, exposure to noise and ototoxic factors, disorders of cholesterol metabolism, arterial hypertension, chronic metabolic disorders (such as diabetes mellitus or kidney diseases), head injuries associated with the loss of consciousness, family history of genetic-related hearing impairment, disorders of the central nervous system, other acute or chronic systemic conditions, and abnormal body mass index (BMI). Moreover, none of the women participating in this study used hormonal preparations. All the participants were white. Mean body height of the study subjects was 172 cm (range 155–190 cm).

The protocol of the study was approved by the Local Bioethics Committee at the Medical University of Silesia (decision no. KNW/0022/KBI/28/09). All the experiments were conducted in accordance with the Declaration of Helsinki (revision 6, 2008) regarding the principles of human experimentation. Written informed consents were obtained from all the participants prior to any procedure included in the study protocol.

The protocol of the study included history-taking, otoscopic examination, tympanometry, PTA, and the evaluation of different types of OAEs.

PTA included air-conduction audiometry at 250–8 000 Hz, bone-conduction audiometry at 250–400 Hz, and ultra-high-frequency PTA at 8 000–20 000 Hz. PTA was performed in a sound-treated room, using an AC-40 Interacoustics Audiometer.

All otoacoustic emission tests (CEOAEs, DPOAEs, and SOAEs) were conducted with an Echoport ILO292 analyzer system, version 6.0 (Otodynamics). Otoacoustic emissions were performed separately for each ear. Prior to the test, the software automatically checked the resonance of the external ear canal and the probe sealing. CEOAEs were recorded in a nonlinear mode with 80-millisecond clicks presented at 85±3 dB pSPL and at a 50 per second rate. Recordings were time-windowed from 2.5 to 20 milliseconds. The responses to a total of 260 sets of clicks were averaged above the noise rejection level of 45 dB. The ILO292 system averages into 2 alternate buffers:

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A and B. The signal is estimated from the (A+B)/2 waveform, and the noise from the A-B difference waveform. The reproducibility is defined as the zero-lag correlation coefficient between the A and B buffers. CEOAEs were measured within the range of 1.0-5.0 kHz; the overall CEOAE response was analyzed.

DPOAEs were measured using a 2-channel probe using the same ILO292 analyzer system. For CEOAEs, a soft adapter was used to provide precise adaptation of the probe to the wall of the external ear canal. The otoacoustic emissions evoked by 2 tonal signals of different frequencies (f_1 and f_2) in a constant relation (f_2/f_1=1.22) were recorded. The levels of primary tones were different: L_1=71 dB SPL and L_2=60 dB SPL (according to Neely's and Gorg's formula: $L_1=44+0.45\times L_2$); the tones were delivered at a constant frequency ratio f_2/f_1=1.22. The DP-grams for $2f_1$-f_2 were collected for the f_2 frequencies of 842 Hz to 7996 Hz with the resolution of 4 points per octave. Subsequently, DPOAEs were tested at the following intensities of primary stimuli, and the distortion $2f_1$–f_2 was analyzed. DPOAEs were tested as a function of DP-gram and the input/output function at L_2=40 dB SPL, 45 dB SPL, 50 dB SPL, 55 dB SPL, 60 dB SPL, 65 dB SPL, and 70 dB SPL. The input/output function was analyzed at 1000 Hz, 1500 Hz, 2000 Hz, 3000 Hz, 4000 Hz, 5000 Hz, and 6000 Hz.

The CEOAEs were considered present at Resp ≥3 dB SPL and Repro >75%, whereas DPOAEs whenever the signal-to-noise ratio (S/N) was higher than at 3 dB, irrespective of frequency. Similar criteria were implemented in the case of SOAEs.

Statistical analysis was carried out with a Statistica 8.0 PL package (StatSoft, United States). Normal distribution of the analyzed variables was verified with the Shapiro-Wilk test. The Student t-test and the Mann-Whitney U-test were used for the intergroup comparisons of normally and non-normally distributed/ranked variables, respectively (non-smokers *vs.* smokers, female non-smokers *vs.* male non-smokers, female non-smokers *vs.* female smokers, male non-smokers *vs.* male smokers, and female smokers *vs.* male smokers). The Bonferroni correction for the repeated measurements was applied.

We did not conduct an ANOVA (except from CEOAE – Repro, Resp, Noise) due to the characteristics of data distribution (lack of normality) and their specific character (the measurements were taken at 5-unit intervals, up to a maximum value). Parametric tests could be used solely for DPOAE-noise.

The results of PTA and ultra-high frequency PTA were recorded to the nearest 5th unit of the interval scale. Due to lack of normal distribution, the Mann-Whitney U-test was used with Bonferroni correction for repeated measurements.

Since the results for DPOAE were not distributed normally, the Mann-Whitney U-test was used with Bonferroni correction for repeated measurements. The only variable with normal distribution was DPOAE (Noise); therefore, the Student t-test was conducted with Bonferroni correction for repeated measurements.

In the case of CEOAE, Resp (dB), Repro (%), and Noise (dB) variables were distributed normally; therefore, the Student t-test was used to compare them. Stab (%) was the only variable without a normal distribution; therefore, the Mann-Whitney U-test was conducted. No Bonferroni correction was used owing to lack of repeated measurements.

The statistical characteristics of the analyzed variables are presented as means and their standard deviations (SD). The threshold of statistical significance for all the tests was set at $p<0.05$.

Results

Hearing threshold assessed with PTA

Smokers and non-smokers did not differ significantly in terms of their hearing thresholds at 250-20 000 Hz. Nevertheless, the smokers presented with slightly higher hearing thresholds at all the frequencies examined ($p>0.05$): PTA thresholds at 250–8 000 (Figures 1–5) and PTA thresholds at ultra-high frequencies (Figures 6–10).

Click-evoked otoacoustic emissions

The levels of CEOAEs is smokers were always lower than in non-smokers, but most of these differences did not prove significant on statistical analysis. The only statistically significant differences in the overall CEOAE levels were found when the results of male smokers were compared with those of male non-smokers ($p=0.026$) and female smokers ($p=0.001$) (Tables 1–5). This suggests that, in contrast to smoking women, male smokers are at increased risk of functional OHC impairment.

Distortion-product otoacoustic emissions (DP-gram function)

The analyzed groups did not differ significantly in terms of their DPOAE levels at various frequencies, both in SNR analysis and when the overall response level was considered. The only exception pertained to the level of DPOAEs at f_2=1 685 Hz, which was significantly lower in male smokers than in male non-smokers. All the results are presented in Tables 6–10. Irrespective of the testing conditions, no significant intergroup differences were found with regards to the background noise level.

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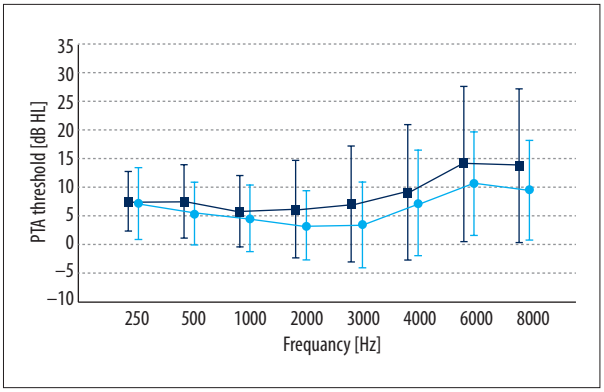

Figure 1. PTA thresholds at 250–8 000 Hz in smokers (squares) and non-smokers (circles).

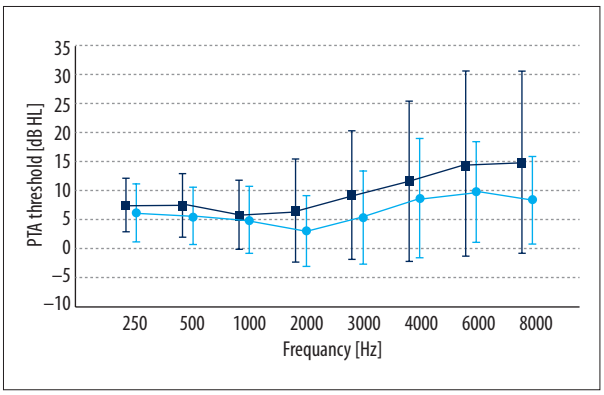

Figure 2. PTA thresholds at 250–8 000 in male smokers (squares) and male non-smokers (circles).

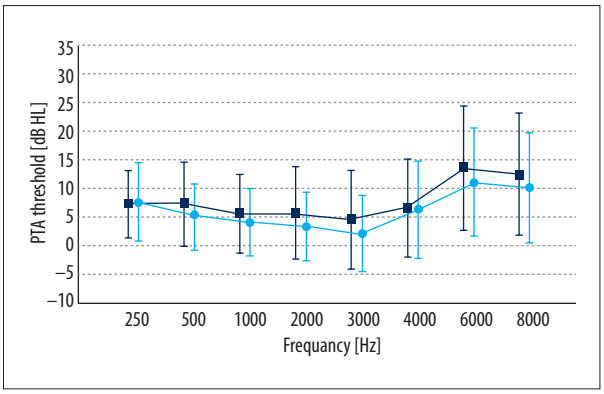

Figure 3. PTA thresholds at 250–8 000 in female smokers (squares) and female non-smokers (circles).

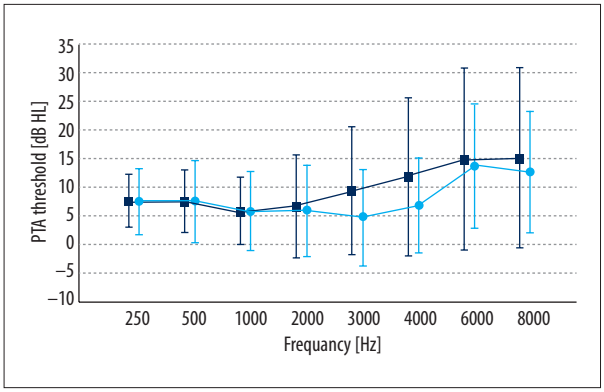

Figure 4. PTA thresholds at 250–8 000 in male smokers (squares) and female smokers (circles).

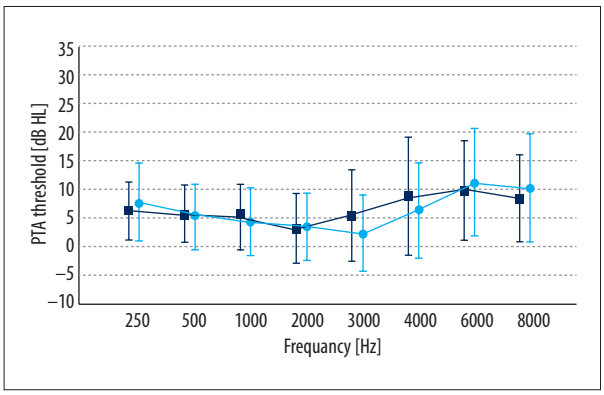

Figure 5. PTA thresholds at 250–8 000 in male non-smokers (squares) and female non-smokers (circles).

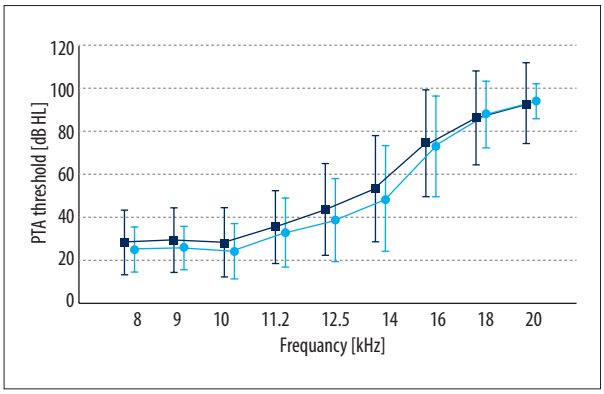

Figure 6. PTA thresholds at high frequencies in smokers (squares) and non-smokers (circles).

Active and passive mechanisms of the cochlea (I/O function of DPOAEs)

Aside from significant differences between smokers and non-smokers overall, we also found significant differences between male smokers and male non-smokers, as well as between male and female smokers. This suggests that smoking may impair the cochlear mechanisms, but predominantly in males. Irrespective of the testing conditions, no significant intergroup differences were found with regards to the background noise level.

Smokers presented with significantly lower levels of DPOAEs than non-smokers at the following frequencies (f_2) and stimulus intensities (L_2): 1000 Hz +60 dB SPL and 45 dB SPL, 1 500 Hz +70 dB SPL, 65 dB SPL, 60 dB SPL and 40 dB SPL, 2 000 Hz

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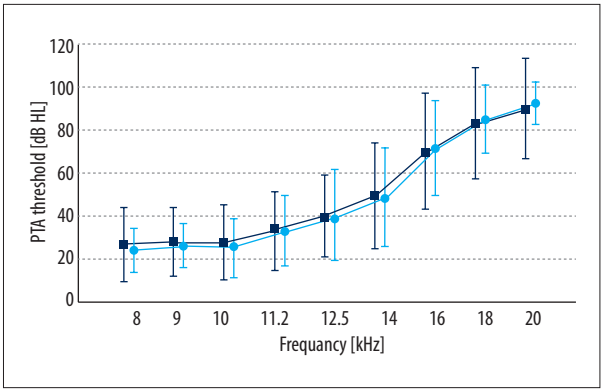

Figure 7. PTA thresholds at high frequencies in male smokers (squares) and male non-smokers (circles).

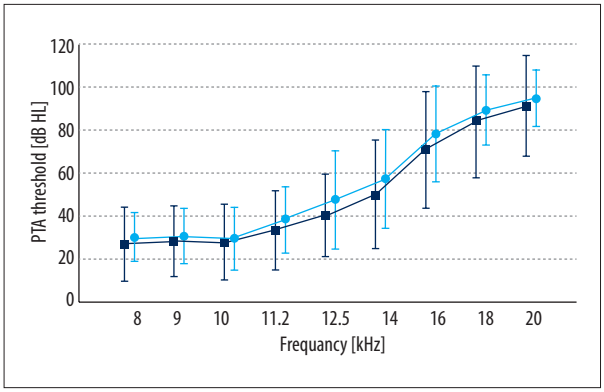

Figure 9. PTA thresholds at high frequencies in male smokers (squares) and female smokers (circles).

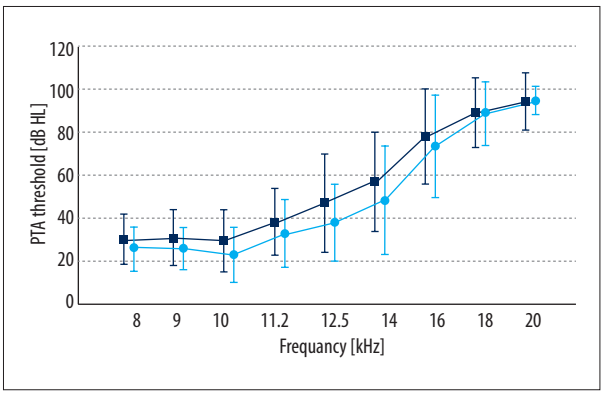

Figure 8. PTA thresholds at high frequencies in female smokers (squares) and female non-smokers (circles).

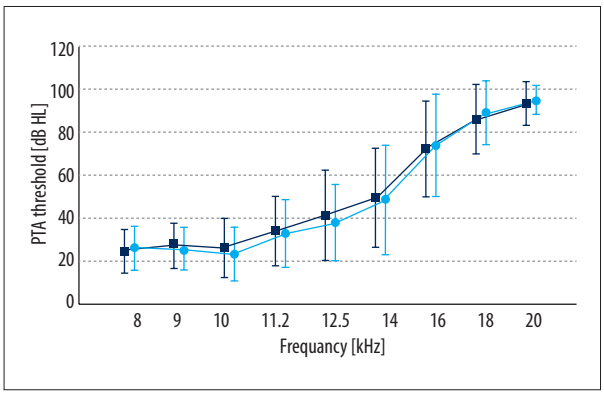

Figure 10. PTA thresholds at high frequencies in male non-smokers (squares) and female non-smokers (circles).

Table 1. CEOAE levels in smokers and non-smokers.

Parameter	Smokers			Non-smokers			p
	n (ears)	Mean	SD	n (ears)	Mean	SD	
Resp dB	81	10.74	4.46	75	10.88	3.63	0.833
Repro %	81	92.59	6.11	75	92.56	6.76	0.975
Noise dB	81	–1.80	3.08	75	–1.65	3.51	0.791
Stab %	81	99.74	0.95	75	99.57	2.69	0.871

Table 2. CEOAE levels in male smokers and female smokers.

Parameter	Male smokers			Female smokers			p
	n (ears)	Mean	SD	n (ears)	Mean	SD	
Resp dB	39	9.13	3.55	42	12.24	4.73	0.001
Repro %	39	90.74	6.82	42	94.31	4.84	0.009
Noise dB	39	–1.80	2.92	42	–1.79	3.25	0.983
Stab %	39	99.85	0.37	42	99.64	1.27	0.760

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Table 3. CEOAE levels in male non-smokers and female non-smokers.

Parameter	Male non-smokers			Female non-smokers			p
	n (ears)	Mean	SD	n (ears)	Mean	SD	
Resp dB	29	11.21	3.86	46	10.67	3.51	0.541
Repro %	29	93.90	5.96	46	91.72	7.16	0.159
Noise dB	29	–2.17	3.71	46	–1.33	3.39	0.329
Stab %	29	99.76	0.44	46	99.46	3.43	0.378

Table 4. CEOAE levels in male smokers and male non-smokers.

Parameter	Male smokers			Male non-smokers			p
	n (ears)	Mean	SD	n (ears)	Mean	SD	
Resp dB	39	9.13	3.55	29	11.21	3.86	0.026
Repro %	39	90.74	6.82	29	93.90	5.96	0.047
Noise dB	39	–1.80	2.92	29	–2.17	3.71	0.662
Stab %	39	99.85	0.37	29	99.76	0.44	0.372

Table 5. CEOAE levels in female smokers and female non-smokers.

Parameter	Female smokers			Female non-smokers			p
	n (ears)	Mean	SD	n (ears)	Mean	SD	
Resp dB	42	12.24	4.73	46	10.67	3.51	0.083
Repro %	42	94.31	4.84	46	91.72	7.16	0.048
Noise dB	42	–1.79	3.25	46	–1.33	3.39	0.520
Stab %	42	99.64	1.27	46	99.46	3.43	0.351

+60 dB SPL or 55 dB SPL, and 3000 Hz +60 dB SPL, 50 dB SPL and 45 dB SPL. These findings suggest that smoking impairs both active and passive mechanisms of the cochlea, especially at lower and moderate frequencies (1–3 kHz).

Compared to male non-smokers, male smokers presented with significantly lower DPOAE levels in an I/O function at the following frequencies (f_2) and stimulus intensities (L_2): 1 000 Hz +60 dB SPL, 50 dB SPL, 45 dB SPL and 40 dB SPL, 1500 Hz +70 dB SPL and 65 dB SPL, 2 000 Hz +70 dB SPL, 65 dB SPL, 60 dB SPL and 55 dB SPL, 3000 Hz +45 dB SPL and 40 dB SPL, and 4000 Hz +70 dB SPL. Unlike in men, female smokers and non-smokers did not differ significantly in terms of their DPOAE levels in an I/O function.

Comparative analysis of male and female smokers showed that the former presented with significantly lower DPOAE levels in an I/O function at the following frequencies (f_2) and stimulus intensities (L_2): 1000 Hz +60 dB SPL, 55 dB SPL, 50 dB SPL and 45 dB SPL, 2000 Hz +70 dB SPL, 65 dB SPL, 60 dB SPL and 40 dB SPL, and 5000 Hz + 70 dB SPL, 60 dB SPL and 55 dB SPL. In contrast, male and female non-smokers did not differ significantly in terms of their DPOAE levels in an I/O function. All the results are presented in Tables 11–15.

Altogether, the aforementioned data suggest that smoking impairs the OHC function in men, but not in women.

Spontaneous otoacoustic emissions

The results of SOAE analysis were consistent with the above-mentioned data on DPOAE levels in an I/O function. Male smokers were at greater risk of toxic OHC impairment than female smokers. SOAEs were observed in 4.3% and 25% of

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Table 6. DPOAE levels in smokers and non-smokers.

Frequency	Smokers						Non-smokers						p DP	p noise	p SNR
	DP		Noise		SNR		DP		Noise		SNR				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
842 Hz	4.19	5.91	–3.81	3.83	7.98	5.94	3.86	6.10	–4.41	3.86	8.27	5.49	1.000	0.996	1.000
1001 Hz	4.18	6.93	–5.84	3.53	10.02	5.87	5.36	7.56	–6.05	3.28	11.41	7.60	0.991	1.000	0.943
1184 Hz	6.77	7.67	–6.11	3.61	12.88	6.97	6.91	6.05	–7.02	3.36	13.92	5.85	1.000	0.737	0.992
1416 Hz	7.76	8.70	–6.58	3.80	14.34	7.73	8.59	8.09	–7.58	3.45	16.06	7.81	1.000	0.670	0.900
1685 Hz	8.28	6.91	–8.12	2.76	16.43	6.46	9.47	6.04	–7.67	2.76	17.14	6.82	0.972	0.990	1.000
2002 Hz	7.26	6.15	–9.12	2.60	16.38	5.77	7.75	7.23	–9.37	2.26	17.12	7.40	1.000	1.000	1.000
2380 Hz	6.10	7.15	–9.53	2.30	15.62	7.05	7.18	6.23	–9.98	2.52	17.16	6.20	0.990	0.967	0.855
2832 Hz	4.83	8.96	–10.31	2.34	15.15	8.15	7.45	6.96	–10.24	1.86	17.69	7.14	0.382	1.000	0.363
3369 Hz	7.31	6.78	–9.78	3.20	17.34	6.45	7.64	6.99	–10.08	1.85	17.72	7.26	1.000	1.000	1.000
4004 Hz	9.11	8.26	–9.77	2.02	19.00	7.92	10.30	6.42	–9.87	1.76	20.09	6.66	0.991	1.000	0.995
4761 Hz	10.11	8.62	–9.50	2.13	19.77	7.91	11.39	7.09	–9.43	2.21	20.83	6.78	0.989	1.000	0.997
5652 Hz	6.87	9.96	–9.25	2.38	16.11	9.17	7.27	8.66	–10.12	2.78	17.26	8.09	1.000	0.334	0.999
6726 Hz	–0.62	10.57	–10.65	3.37	10.26	9.68	0.75	10.58	–11.39	2.60	12.14	9.95	0.999	0.811	0.967
7996 Hz	–15.35	13.27	–13.13	2.13	–1.68	12.55	–12.17	13.10	–13.92	2.48	1.35	11.53	0.873	0.437	0.839

Table 7. DPOAE levels in male smokers and female smokers.

Frequency	Male smokers						Female smokers						p DP	p noise	p SNR
	DP		Noise		SNR		DP		Noise		SNR				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
842 Hz	2.93	6.21	–3.62	4.21	6.51	6.47	5.50	5.37	–4.00	3.44	9.50	4.99	0.546	1.000	0.309
1001 Hz	2.89	6.02	–5.76	3.02	8.65	5.40	5.59	7.64	–5.93	4.07	11.52	6.06	0.652	1.000	0.278
1184 Hz	5.51	7.71	–6.12	3.10	11.63	7.13	8.07	7.50	–6.09	4.10	14.16	6.64	0.834	1.000	0.740
1416 Hz	5.82	9.81	–6.86	3.68	12.69	8.14	9.75	6.97	–6.30	3.94	16.05	6.98	0.422	1.000	0.483
1685 Hz	6.73	6.57	–8.30	2.74	15.10	5.93	9.86	6.96	–7.94	2.79	17.80	6.77	0.379	1.000	0.515
2002 Hz	6.14	5.56	–9.06	2.49	15.20	5.46	8.40	6.58	–9.19	2.74	17.59	5.90	0.710	1.000	0.529
2380 Hz	4.68	7.01	–9.63	1.96	14.31	6.82	7.55	7.07	–9.42	2.62	16.97	7.11	0.578	1.000	0.672
2832 Hz	4.05	9.39	–10.22	2.58	14.28	8.48	5.64	8.54	–10.41	2.10	16.07	7.78	0.999	1.000	0.992
3369 Hz	6.53	6.82	–9.48	3.78	16.50	6.90	8.10	6.74	–10.09	2.50	18.19	5.92	0.987	0.998	0.966
4004 Hz	7.84	9.45	–9.56	1.73	17.63	9.13	10.41	6.71	–9.98	2.27	20.39	6.25	0.882	0.996	0.774
4761 Hz	8.55	9.49	–9.72	2.31	18.27	9.01	11.75	7.36	–9.28	1.91	21.34	6.30	0.682	0.996	0.610
5652 Hz	5.98	9.67	–8.77	2.01	14.75	9.21	7.80	10.29	–9.74	2.65	17.54	9.01	0.999	0.566	0.902
6726 Hz	–0.96	9.67	–9.98	3.89	9.48	8.97	–0.26	11.57	–11.36	2.55	11.11	10.44	1.000	0.556	1.000
7996 Hz	–15.24	13.81	–13.12	2.23	–2.11	12.78	–15.46	12.90	–13.14	2.07	–1.26	12.48	1.000	1.000	1.000

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Table 8. DPOAE levels in male non-smokers and female non-smokers.

Frequency	Male non-smokers						Female non-smokers						p DP	p noise	p SNR
	DP		Noise		SNR		DP		Noise		SNR				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
842 Hz	5.47	6.35	–3.71	4.14	9.18	6.29	2.71	5.71	–4.90	3.61	7.61	4.82	0.572	0.954	0.979
1001 Hz	6.37	9.49	–5.24	3.81	11.61	9.71	4.75	6.14	–6.54	2.84	11.29	6.09	0.999	0.807	1.000
1184 Hz	7.16	6.40	–7.08	3.99	14.24	6.46	6.75	5.88	–6.98	2.92	13.71	5.48	1.000	1.000	1.000
1416 Hz	9.23	7.53	–7.11	3.45	16.05	8.35	8.19	8.48	–7.88	3.45	16.08	7.54	1.000	0.995	1.000
1685 Hz	11.42	5.02	–8.00	3.06	19.42	5.91	8.30	6.34	–7.47	2.58	15.77	7.01	0.204	0.999	0.179
2002 Hz	9.06	8.03	–8.80	2.09	17.86	8.80	6.95	6.64	–9.72	2.30	16.67	6.44	0.964	0.602	1.000
2380 Hz	7.09	7.27	–9.97	2.50	17.06	7.49	7.23	5.57	–9.98	2.55	17.22	5.34	1.000	1.000	1.000
2832 Hz	6.88	9.86	–10.75	1.68	17.64	10.17	7.80	4.30	–9.92	1.91	17.72	4.40	1.000	0.443	1.000
3369 Hz	7.22	8.76	–10.00	1.82	17.22	8.95	7.91	5.67	–10.14	1.89	18.05	6.01	1.000	1.000	1.000
4004 Hz	9.74	7.93	–9.78	1.77	19.32	8.19	10.64	5.33	–9.93	1.77	20.57	5.55	1.000	1.000	1.000
4761 Hz	10.91	6.83	–9.27	2.14	20.18	6.58	11.69	7.30	–9.53	2.27	21.23	6.94	1.000	1.000	1.000
5652 Hz	6.76	9.10	–10.14	2.68	16.90	8.43	7.59	8.45	–10.11	2.86	17.48	7.95	1.000	1.000	1.000
6726 Hz	–0.90	12.07	–11.48	2.95	10.58	10.74	1.92	9.35	–11.33	2.36	13.24	9.31	0.985	1.000	0.981
7996 Hz	–11.06	12.84	–14.39	2.57	3.33	11.75	–12.79	13.35	–13.65	2.42	0.22	11.38	1.000	0.971	0.986

Table 9. DPOAE levels in male smokers and male non-smokers.

Frequency	Male smokers						Male non-smokers						p DP	p noise	p SNR
	DP		Noise		SNR		DP		Noise		SNR				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
842 Hz	2.93	6.21	–3.62	4.21	6.51	6.47	5.47	6.35	–3.71	4.14	9.18	6.29	0.758	1.000	0.711
1001 Hz	2.89	6.02	–5.76	3.02	8.65	5.40	6.37	9.49	–5.24	3.81	11.61	9.71	0.690	1.000	0.864
1184 Hz	5.51	7.71	–6.12	3.10	11.63	7.13	7.16	6.40	–7.08	3.99	14.24	6.46	0.994	0.984	0.774
1416 Hz	5.82	9.81	–6.86	3.68	12.69	8.14	9.23	7.53	–7.11	3.45	16.05	8.35	0.748	1.000	0.716
1685 Hz	6.73	6.57	–8.30	2.74	15.10	5.93	11.42	5.02	–8.00	3.06	19.42	5.91	**0.012**	1.000	**0.040**
2002 Hz	6.14	5.56	–9.06	2.49	15.20	5.46	9.06	8.03	–8.80	2.09	17.86	8.80	0.694	1.000	0.867
2380 Hz	4.68	7.01	–9.63	1.96	14.31	6.82	7.09	7.27	–9.97	2.50	17.06	7.49	0.892	1.000	0.781
2832 Hz	4.05	9.39	–10.22	2.58	14.28	8.48	6.88	9.86	–10.75	1.68	17.64	10.17	0.958	0.985	0.853
3369 Hz	6.53	6.82	–9.48	3.78	16.50	6.90	7.22	8.76	–10.00	1.82	17.22	8.95	1.000	0.999	1.000
4004 Hz	7.84	9.45	–9.56	1.73	17.63	9.13	9.74	7.93	–9.78	1.77	19.32	8.19	0.997	1.000	0.999
4761 Hz	8.55	9.49	–9.72	2.31	18.27	9.01	10.91	6.83	–9.27	2.14	20.18	6.58	0.957	0.999	0.989
5652 Hz	5.98	9.67	–8.77	2.01	14.75	9.21	6.76	9.10	–10.14	2.68	16.90	8.43	1.000	0.227	0.991
6726 Hz	–0.96	9.67	–9.98	3.89	9.48	8.97	–0.90	12.07	–11.48	2.95	10.58	10.74	1.000	0.571	1.000
7996 Hz	–15.24	13.81	–13.12	2.23	–2.11	12.78	–11.06	12.84	–14.39	2.57	3.33	11.75	0.962	0.474	0.693

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Table 10. DPOAE levels in female smokers and female non-smokers.

Frequency	Female smokers						Female non-smokers						p DP	p noise	p SNR
	DP		Noise		SNR		DP		Noise		SNR				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
842 Hz	5.50	5.37	–4.00	3.44	9.50	4.99	2.71	5.71	–4.90	3.61	7.61	4.82	0.311	0.980	0.717
1001 Hz	5.59	7.64	–5.93	4.07	11.52	6.06	4.75	6.14	–6.54	2.84	11.29	6.09	1.000	0.999	1.000
1184 Hz	8.07	7.50	–6.09	4.10	14.16	6.64	6.75	5.88	–6.98	2.92	13.71	5.48	0.997	0.976	1.000
1416 Hz	9.75	6.97	–6.30	3.94	16.05	6.98	8.19	8.48	–7.88	3.45	16.08	7.54	0.996	0.482	1.000
1685 Hz	9.86	6.96	–7.94	2.79	17.80	6.77	8.30	6.34	–7.47	2.58	15.77	7.01	0.982	0.999	0.901
2002 Hz	8.40	6.58	–9.19	2.74	17.59	5.90	6.95	6.64	–9.72	2.30	16.67	6.44	0.989	0.993	1.000
2380 Hz	7.55	7.07	–9.42	2.62	16.97	7.11	7.23	5.57	–9.98	2.55	17.22	5.34	1.000	0.991	1.000
2832 Hz	5.64	8.54	–10.41	2.10	16.07	7.78	7.80	4.30	–9.92	1.91	17.72	4.40	0.863	0.976	0.965
3369 Hz	8.10	6.74	–10.09	2.50	18.19	5.92	7.91	5.67	–10.14	1.89	18.05	6.01	1.000	1.000	1.000
4004 Hz	10.41	6.71	–9.98	2.27	20.39	6.25	10.64	5.33	–9.93	1.77	20.57	5.55	1.000	1.000	1.000
4761 Hz	11.75	7.36	–9.28	1.91	21.34	6.30	11.69	7.30	–9.53	2.27	21.23	6.94	1.000	1.000	1.000
5652 Hz	7.80	10.29	–9.74	2.65	17.54	9.01	7.59	8.45	–10.11	2.86	17.48	7.95	1.000	1.000	1.000
6726 Hz	–0.26	11.57	–11.36	2.55	11.11	10.44	1.92	9.35	–11.33	2.36	13.24	9.31	0.996	1.000	0.994
7996 Hz	–15.46	12.90	–13.14	2.07	–1.26	12.48	–12.79	13.35	–13.65	2.42	0.22	11.38	0.997	0.991	1.000

male smokers and non-smokers, respectively, and in 47.6% and 60.5% of female smokers and non-smokers, respectively. This clearly shows that men are more susceptible to smoking-induced hearing impairment.

Discussion

The effects of isolated exposure to tobacco smoke are extremely difficult to determine because smokers are frequently co-exposed to other ototoxic factors, especially in an occupational setting [18–20]. Moreover, the differences in male and female physiology should be considered; namely, the potential protective effect of hormonal factors on the female hearing organ [21,22]. Finally, the accurate evaluation of the hearing effects requires a group of individuals with sufficiently long and extensive exposure to the components of tobacco smoke. Furthermore, the selection of an appropriate method for hearing examination is an important issue since not every test is suitable for detection of changes at a subclinical level. Evaluation of otoacoustic emissions is an objective and highly sensitive method for hearing assessment [16–18,23,24]. The sensitivity of this test can be improved by the use of various intensities of L_1 and L_2 stimuli, as well as by the implementation of an input/output function [24–26].

The smokers and non-smokers participating in our study did not differ significantly in terms of their results of PTA at a 250–20 000 Hz frequency range. However, despite the lack of statistically significant differences, the hearing threshold of smokers was slightly higher than in non-smokers. This observation is consistent with the data published recently by Negley et al. [26]. Although the hearing threshold at a standard spectrum did not exceed 25 dB HL in any of the subjects participating in this study, the smokers presented with a 2–10 dB higher hearing thresholds than the controls. However, the smokers and non-smokers did not differ significantly in terms of their hearing thresholds at high frequencies [26]. In contrast, Paschoal and Azevedo [27] found significant differences in the audiometric hearing thresholds of smokers and non-smokers at 8 kHz, 12.5 kHz, and 14 kHz. Also, Oliveira and Lima [28] showed that the individuals who smoked for at least 5 years presented with significantly higher (albeit within a normal limit) hearing thresholds at a standard spectrum and at high frequencies than the subjects who never smoked. However, this study involved a relatively small sample of smokers (n=30), and its authors did not provide information about the daily number of cigarettes smoked in this group [28]. Basar and Belgin [29] examined 30 individuals with a 10-year history of smoking at least 1 package per day and 20 non-smoking controls, and found that the former presented with significantly higher hearing thresholds solely at 16 kHz and 18 kHz. Sousa et al. [30]

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Table 11. DPOAE levels – I/O analysis in smokers and non-smokers.

L2 level dB SPL	Smokers			Non smokers			p	Smokers			Non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	1000 Hz DPOAE levels							1000 Hz SNR analysis						
70	82	9.38	5.95	80	9.67	6.69	0.766	82	12.19	5.56	80	13.06	6.64	0.368
65	84	6.88	6.96	81	7.31	5.86	0.666	84	9.61	6.01	81	10.86	6.23	0.192
60	84	6.14	7.34	78	7.16	5.33	0.319	84	8.81	6.82	78	11.03	5.77	0.027
55	82	5.08	6.32	77	5.43	7.12	0.745	82	9.15	5.75	77	9.82	6.31	0.482
50	79	3.27	6.61	75	3.76	7.58	0.675	79	8.00	6.25	75	9.18	7.16	0.276
45	75	0.96	7.04	72	2.79	6.11	0.095	75	6.09	6.40	72	8.44	5.83	0.022
40	64	–2.44	9.69	68	–0.73	8.43	0.282	64	3.34	8.17	68	5.55	7.54	0.108
	1500 Hz DPOAE levels							1500 Hz SNR analysis						
70	85	11.92	7.65	81	13.49	5.45	0.131	85	16.80	7.85	81	20.38	6.41	0.002
65	84	10.70	8.33	80	12.41	5.30	0.122	84	15.39	8.00	80	18.17	5.95	0.013
60	85	9.56	7.09	79	10.97	5.88	0.169	85	14.76	6.19	79	16.75	5.99	0.039
55	84	7.55	8.04	80	8.53	8.26	0.441	84	13.26	7.18	80	14.63	7.76	0.242
50	83	5.22	8.62	80	6.47	7.52	0.324	83	11.40	7.05	80	12.92	6.86	0.167
45	79	3.38	7.79	79	4.95	7.28	0.192	79	10.34	5.99	79	12.07	6.84	0.094
40	76	0.02	9.63	78	1.82	8.62	0.223	76	7.04	7.82	78	9.83	7.81	0.028
	2000 Hz DPOAE levels							2000 Hz SNR analysis						
70	86	11.90	5.31	81	12.07	5.78	0.841	86	19.75	6.33	81	21.27	6.28	0.122
65	86	10.89	5.51	81	11.24	5.81	0.690	86	18.00	6.06	81	19.65	6.13	0.082
60	86	8.67	7.43	80	10.16	6.17	0.163	86	16.23	7.35	80	18.60	6.81	0.033
55	84	7.62	5.92	81	8.23	6.35	0.523	84	15.34	6.07	81	17.41	6.45	0.035
50	84	4.93	7.56	79	6.03	7.65	0.358	84	13.55	7.18	79	15.03	7.57	0.202
45	83	2.90	6.44	80	2.88	8.68	0.984	83	11.77	6.17	80	12.63	7.76	0.431
40	76	0.05	7.73	79	–1.13	10.40	0.426	76	8.88	6.36	79	8.86	9.63	0.991
	3000 Hz DPOAE levels							3000 Hz SNR analysis						
70	85	10.19	5.57	81	11.08	5.67	0.310	85	20.45	5.85	81	22.11	6.07	0.073
65	85	9.18	6.23	81	9.93	6.50	0.446	85	18.54	6.13	81	19.81	6.93	0.210
60	86	7.42	6.41	81	8.69	5.84	0.184	86	16.59	6.54	81	18.60	5.83	0.038
55	86	5.98	7.22	82	7.20	7.27	0.277	86	15.56	6.73	82	17.20	7.30	0.130
50	86	3.94	8.12	82	5.65	6.34	0.131	86	13.89	6.77	82	15.84	5.93	0.049
45	83	0.29	11.46	82	2.79	7.70	0.102	83	10.43	9.64	82	13.76	7.59	0.015
40	79	–0.98	10.26	80	0.65	7.27	0.248	79	10.07	8.55	80	11.66	6.73	0.196

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Table 11 continued. DPOAE levels – I/O analysis in smokers and non-smokers.

L2 level dB SPL	Smokers			Non smokers			p	Smokers			Non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	4000 Hz DPOAE levels							4000 Hz SNR analysis						
70	86	13.74	6.29	80	14.38	5.18	0.475	86	23.71	6.70	80	25.52	5.45	0.060
65	86	12.66	6.58	80	13.40	5.07	0.422	86	21.85	6.68	80	23.60	5.04	0.061
60	85	11.25	6.83	81	11.62	6.00	0.709	85	20.86	6.73	81	21.54	6.29	0.502
55	84	9.91	7.63	81	10.25	6.25	0.757	84	19.36	7.17	81	20.09	6.02	0.476
50	86	7.21	9.42	81	8.41	5.95	0.331	86	17.24	8.60	81	18.61	5.76	0.232
45	85	4.47	10.40	81	5.79	7.47	0.352	85	14.42	9.01	81	16.15	6.94	0.170
40	84	1.75	10.99	80	3.59	6.80	0.203	84	11.57	9.47	80	13.73	6.58	0.094
	5000 Hz DPOAE levels							5000 Hz SNR analysis						
70	85	14.12	8.10	82	14.30	7.37	0.883	85	23.75	7.56	82	25.00	7.17	0.276
65	85	12.37	7.57	82	12.09	8.38	0.816	85	21.32	7.18	82	21.81	7.50	0.671
60	86	10.85	7.95	82	10.84	8.72	0.991	86	19.92	7.53	82	20.60	8.09	0.572
55	85	8.78	7.99	81	9.46	7.15	0.566	85	18.07	6.98	81	19.15	5.91	0.287
50	84	5.99	9.37	82	6.47	8.89	0.735	84	15.80	7.61	82	16.54	7.91	0.539
45	85	3.22	10.48	82	4.40	9.59	0.450	85	13.46	8.52	82	14.71	8.55	0.343
40	83	–0.18	11.95	80	2.45	7.68	0.098	83	9.96	9.92	80	12.58	6.81	0.052
	6000 Hz DPOAE levels							6000 Hz SNR analysis						
70	86	13.56	9.39	82	14.05	7.72	0.717	86	23.99	9.39	82	25.08	7.79	0.418
65	84	12.22	8.22	80	12.53	7.62	0.801	84	21.77	7.71	80	22.51	7.38	0.534
60	86	9.02	10.01	80	10.09	7.46	0.441	86	18.92	8.74	80	19.98	7.01	0.389
55	83	6.63	11.00	81	6.85	8.48	0.885	83	16.78	9.51	81	16.94	8.00	0.905
50	84	2.36	13.19	81	4.01	8.68	0.346	84	12.78	11.43	81	14.85	7.46	0.173
45	81	–0.32	12.88	80	0.25	9.64	0.751	81	10.01	10.71	80	11.48	8.55	0.340
40	78	–4.29	13.35	73	–4.02	11.54	0.893	78	6.65	10.90	73	7.72	9.80	0.528

analyzed the exposure of 625 volunteers to various risk factors of hearing impairment. Neither PTA nor speech audiometry confirmed the role of tobacco smoking as a risk factor for this condition [30]. The influence of tobacco smoking and noise on hearing, examined by means of tone audiometry at a standard spectrum, was also analyzed by Pouryaghoub et al. [20]; they found that a group of 206 smokers was characterized by significantly higher hearing threshold at 4 kHz when compared to 206 non-smoking controls.

Aside from smoking, the hearing impairment documented in some of our participants might be related to their sex, age (up to 67 years), and/or exposure to noise [20]. An important study analyzing the effect of sex on the auditory consequences of smoking was conducted by Uchida et al. [31]. They found that the results of PTA at 4000 Hz were significantly worse in male smokers than in male non-smokers, but a similar phenomenon was not observed in the case of female smokers and non-smokers [31]. Nomura et al. [32] conducted a meta-analysis of 15 studies published between 1966 and 2003, in order to determine the effects of cigarette smoking on the results of

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Table 12. DPOAE levels – I/O analysis in male smokers and female smokers.

L2 level dB SPL	Male smokers			Female smokers			p	Male smokers			Female smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	1000 Hz DPOAE levels							1000 Hz SNR analysis						
70	40	9.74	5.51	42	9.03	6.38	0.590	40	12.25	5.66	42	12.13	5.53	0.924
65	43	5.76	7.02	41	8.06	6.77	0.131	43	8.38	6.74	41	10.90	4.90	0.053
60	43	4.67	7.71	41	7.69	6.69	0.058	43	7.17	7.39	41	10.54	5.75	0.022
55	41	3.60	6.08	41	6.56	6.29	0.034	41	7.77	6.16	41	10.52	5.03	0.030
50	40	1.93	6.26	39	4.66	6.75	0.067	40	6.04	6.81	39	10.01	4.94	0.004
45	36	–0.69	6.72	39	2.48	7.07	0.050	36	4.43	7.16	39	7.62	5.25	0.033
40	30	–3.44	9.07	34	–1.55	10.25	0.436	30	2.15	7.46	34	4.39	8.71	0.273
	1500 Hz DPOAE levels							1500 Hz SNR analysis						
70	44	10.49	7.26	41	13.45	7.84	0.075	44	15.90	7.55	41	17.77	8.15	0.276
65	43	8.81	8.90	41	12.68	7.28	0.032	43	13.91	8.32	41	16.93	7.42	0.083
60	43	8.08	6.13	42	11.07	7.73	0.052	43	14.12	5.59	42	15.42	6.75	0.339
55	42	6.01	6.61	42	9.09	9.08	0.080	42	12.15	6.21	42	14.37	7.95	0.157
50	42	2.74	9.62	41	7.75	6.67	0.007	42	9.92	7.78	41	12.92	5.93	0.051
45	39	2.18	6.28	40	4.54	8.95	0.178	39	10.14	5.29	40	10.55	6.65	0.764
40	42	–1.66	8.57	34	2.10	10.57	0.099	42	6.31	7.80	34	7.94	7.86	0.370
	2000 Hz DPOAE levels							2000 Hz SNR analysis						
70	44	10.66	4.62	42	13.20	5.72	0.026	44	18.10	5.84	42	21.49	6.43	0.012
65	44	9.51	4.98	42	12.33	5.72	0.017	44	16.67	6.09	42	19.40	5.76	0.035
60	44	6.83	8.19	42	10.60	6.06	0.017	44	14.44	8.20	42	18.10	5.87	0.020
55	42	6.57	5.41	42	8.66	6.27	0.106	42	14.45	5.96	42	16.23	6.12	0.182
50	43	3.24	8.31	41	6.70	6.31	0.034	43	12.20	7.94	41	14.96	6.06	0.076
45	42	1.58	5.96	41	4.27	6.70	0.057	42	10.74	6.96	41	12.81	5.11	0.126
40	38	–2.09	8.18	38	2.19	6.70	0.015	38	7.10	6.77	38	10.65	5.43	0.014
	3000 Hz DPOAE levels							3000 Hz SNR analysis						
70	43	9.85	5.04	42	10.54	6.11	0.571	43	20.00	5.28	50	22.41	4.57	0.481
65	43	8.54	6.36	42	9.83	6.11	0.342	43	17.62	6.58	50	20.05	4.29	0.165
60	44	6.68	6.55	42	8.20	6.24	0.274	44	15.82	6.91	50	18.63	5.19	0.261
55	44	4.91	7.98	42	7.11	6.23	0.157	44	14.46	7.23	50	17.67	4.78	0.121
50	44	2.78	8.99	42	5.15	7.00	0.175	44	12.78	7.71	50	15.86	4.51	0.119
45	43	–0.87	12.06	40	1.53	10.80	0.343	43	9.27	10.39	50	13.73	7.21	0.258
40	40	–3.29	12.61	39	1.38	6.45	0.042	40	8.29	10.72	50	10.95	7.13	0.060

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Table 12 continued. DPOAE levels – I/O analysis in male smokers and female smokers.

L2 level dB SPL	Male smokers			Female smokers			p	Male smokers			Female smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	4000 Hz DPOAE levels							4000 Hz SNR analysis						
70	44	13.07	6.77	42	14.44	5.75	0.311	44	22.68	6.93	42	24.79	6.36	0.144
65	44	11.84	7.18	42	13.52	5.85	0.239	44	21.05	7.24	42	22.70	6.01	0.253
60	43	10.61	7.37	42	11.90	6.24	0.385	43	19.72	7.49	42	22.03	5.72	0.114
55	42	9.20	8.56	42	10.61	6.60	0.401	42	18.21	7.96	42	20.50	6.15	0.145
50	44	6.09	9.99	42	8.40	8.75	0.257	44	16.17	9.46	42	18.37	7.55	0.234
45	43	3.41	11.15	42	5.55	9.59	0.346	43	13.21	10.03	42	15.65	7.75	0.213
40	42	0.84	11.43	42	2.67	10.59	0.450	42	10.51	10.06	42	12.62	8.85	0.309
	5000 Hz DPOAE levels							5000 Hz SNR analysis						
70	43	12.76	8.53	42	15.52	7.48	0.116	43	21.97	7.79	42	25.57	6.95	0.027
65	43	11.14	7.53	42	13.63	7.49	0.130	43	20.09	7.50	42	22.58	6.69	0.110
60	44	9.43	8.43	42	12.35	7.21	0.087	44	18.12	8.00	42	21.80	6.58	0.022
55	43	7.67	8.23	42	9.92	7.66	0.195	43	16.52	7.40	42	19.66	6.22	0.037
50	43	4.60	9.43	41	7.44	9.21	0.166	43	14.65	7.89	41	17.00	7.20	0.158
45	43	2.43	10.38	42	4.03	10.65	0.487	43	12.44	8.57	42	14.50	8.44	0.270
40	42	–1.00	11.57	41	0.66	12.41	0.531	42	9.18	9.45	41	10.76	10.43	0.470
	6000 Hz DPOAE levels							6000 Hz SNR analysis						
70	44	12.35	10.25	42	14.84	8.32	0.219	44	22.65	10.64	42	25.40	7.74	0.174
65	42	11.75	8.10	42	12.69	8.41	0.600	42	21.18	7.72	42	22.36	7.74	0.483
60	44	7.71	10.69	42	10.40	9.16	0.214	44	17.61	9.69	42	20.28	7.49	0.156
55	43	5.73	10.40	40	7.59	11.66	0.446	43	15.62	9.31	40	18.03	9.68	0.252
50	43	1.76	12.21	41	2.99	14.27	0.671	43	12.29	10.90	41	13.30	12.07	0.690
45	42	–2.10	13.28	39	1.59	12.31	0.197	42	8.59	11.32	39	11.55	9.94	0.214
40	38	–5.92	13.34	40	–2.75	13.34	0.297	38	5.13	11.00	40	8.09	10.74	0.232

PTA. They documented the unfavorable effect of smoking in 9 out of the 15 analyzed studies; the lack of such an association in the remaining studies suggests that the relationship between smoking and hearing impairment is still not completely understood [32].

Previous research on click-evoked otoacoustic emissions [27,33,34] showed that smokers present with lower CEOAE levels than non-smokers. Paschoal and Azevedo [27] did not observe CEOAEs in 13.9% and 2.8% of smokers and non-smokers, respectively (p=0.016). The levels of CEOAEs do not seem to be modulated by the age of smokers [34]. Interestingly, a study of CEOAEs in newborns whose mothers smoked during pregnancy demonstrated not only the functional impairment of sound perception, but also the structural abnormalities of the hearing organ [33]. In our study, male smokers presented with significantly lower CEOAE levels than male non-smokers and female smokers. To the best of our knowledge, this was the first study to demonstrate sex-specific differences in smokers' CEOAE levels.

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Table 13. DPOAE levels – I/O analysis in male non-smokers and female non-smokers.

L2 level dB SPL	Male non-smokers			Female non-smokers			p	Male non-smokers			Female non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	1000 Hz DPOAE levels							1000 Hz SNR analysis						
70	31	9.83	8.57	49	9.57	5.27	0.880	31	12.63	7.85	49	13.33	5.81	0.320
65	32	8.21	5.87	49	6.73	5.83	0.269	32	11.06	7.22	49	10.73	5.57	0.880
60	29	8.33	4.62	49	6.46	5.63	0.115	29	11.76	5.33	49	10.60	6.02	0.957
55	31	5.87	8.67	46	5.13	5.94	0.677	31	9.38	8.29	46	10.12	4.60	0.695
50	30	5.32	6.36	45	2.72	8.19	0.127	30	10.01	5.25	45	8.63	8.20	0.362
45	30	3.34	7.00	42	2.40	5.44	0.543	30	8.47	6.32	42	8.41	5.54	0.513
40	26	1.72	6.14	42	–2.25	9.33	0.038	26	6.82	6.45	42	4.77	8.11	0.844
	1500 Hz DPOAE levels							1500 Hz SNR analysis						
70	32	13.85	5.59	49	13.26	5.40	0.637	32	20.27	7.03	49	20.45	6.05	0.903
65	32	12.62	5.65	48	12.27	5.10	0.779	32	18.24	6.16	48	18.13	5.88	0.936
60	32	10.89	6.76	47	11.03	5.28	0.923	32	16.56	6.29	47	16.87	5.84	0.824
55	31	9.36	7.33	49	8.01	8.82	0.460	31	15.29	7.75	49	14.21	7.82	0.549
50	31	7.14	8.11	49	6.05	7.18	0.541	31	13.34	7.22	49	12.65	6.69	0.670
45	30	6.17	6.96	49	4.20	7.44	0.238	30	12.81	6.40	49	11.62	7.12	0.446
40	29	1.99	10.67	49	1.72	7.26	0.905	29	9.46	9.80	49	10.05	6.46	0.775
	2000 Hz DPOAE levels							2000 Hz SNR analysis						
70	31	13.19	6.17	50	11.38	5.47	0.185	31	22.45	6.30	50	20.54	6.22	0.188
65	31	12.13	6.36	50	10.68	5.44	0.296	31	20.03	6.69	50	19.42	5.81	0.676
60	30	11.11	7.14	50	9.59	5.50	0.320	30	19.36	7.74	50	18.15	6.22	0.471
55	31	9.12	7.52	50	7.68	5.50	0.361	31	18.53	7.56	50	16.72	5.63	0.255
50	30	6.76	10.01	49	5.58	5.82	0.560	30	15.22	10.43	49	14.91	5.22	0.881
45	31	4.22	8.15	49	2.03	8.98	0.264	31	13.34	7.77	49	12.19	7.80	0.522
40	31	–0.37	10.73	48	–1.61	10.26	0.611	31	9.02	10.26	48	8.76	9.32	0.911
	3000 Hz DPOAE levels							3000 Hz SNR analysis						
70	31	11.26	7.17	50	10.97	4.58	0.844	31	21.63	7.99	50	22.41	4.57	0.624
65	31	9.72	8.91	50	10.07	4.50	0.841	31	19.43	9.88	50	20.05	4.29	0.739
60	31	8.86	6.90	50	8.58	5.15	0.846	31	18.54	6.83	50	18.63	5.19	0.949
55	32	6.89	9.75	50	7.41	5.22	0.783	32	16.47	10.11	50	17.67	4.78	0.534
50	32	5.70	7.58	50	5.61	5.48	0.953	32	15.81	7.73	50	15.86	4.51	0.974
45	32	3.32	7.56	50	2.46	7.84	0.623	32	13.82	8.26	50	13.73	7.21	0.960
40	30	2.34	5.53	50	–0.37	8.02	0.078	30	12.83	5.94	50	10.95	7.13	0.208

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Table 13 continued. DPOAE levels – I/O analysis in male non-smokers and female non-smokers.

L2 level dB SPL	Male non-smokers			Female non-smokers			p	Male non-smokers			Female non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	4000 Hz DPOAE levels							4000 Hz SNR analysis						
70	30	14.84	5.11	50	14.11	5.26	0.544	30	25.95	5.40	50	25.26	5.52	0.585
65	30	13.70	5.12	50	13.22	5.08	0.684	30	23.71	4.50	50	23.53	5.37	0.875
60	31	11.23	7.24	50	11.87	5.15	0.672	31	20.81	7.77	50	22.00	5.21	0.453
55	31	9.94	7.31	50	10.43	5.56	0.749	31	18.97	7.30	50	20.79	5.02	0.229
50	31	8.09	6.64	50	8.61	5.54	0.716	31	17.69	6.83	50	19.18	4.98	0.298
45	31	5.62	7.40	50	5.89	7.59	0.875	31	15.45	7.62	50	16.58	6.54	0.500
40	32	2.76	7.67	48	4.14	6.17	0.397	32	12.48	7.47	48	14.55	5.84	0.191
	5000 Hz DPOAE levels							5000 Hz SNR analysis						
70	32	13.56	8.61	50	14.77	6.51	0.497	32	24.26	8.35	50	25.47	6.35	0.488
65	32	11.25	9.94	50	12.62	7.27	0.504	32	20.91	9.20	50	22.38	6.20	0.428
60	32	10.38	8.61	50	11.14	8.86	0.702	32	19.69	8.46	50	21.18	7.87	0.425
55	31	9.47	6.42	50	9.45	7.64	0.989	31	18.73	5.27	50	19.41	6.31	0.603
50	32	5.48	9.93	50	7.10	8.19	0.443	32	15.65	9.17	50	17.11	7.03	0.447
45	32	2.81	11.40	50	5.42	8.20	0.266	32	12.96	10.75	50	15.84	6.67	0.182
40	31	1.00	8.67	49	3.36	6.92	0.207	31	10.94	7.08	49	13.62	6.50	0.093
	6000 Hz DPOAE levels							6000 Hz SNR analysis						
70	32	14.22	8.87	50	13.93	6.97	0.878	32	24.90	8.76	50	25.19	7.20	0.875
65	30	13.36	8.64	50	12.04	6.98	0.480	30	22.99	8.57	50	22.22	6.65	0.675
60	30	11.31	6.75	50	9.35	7.83	0.241	30	20.69	6.87	50	19.56	7.13	0.485
55	32	6.76	10.18	49	6.91	7.27	0.944	32	15.87	10.15	49	17.64	6.23	0.381
50	32	4.40	8.46	49	3.75	8.90	0.743	32	14.60	8.04	49	15.01	7.14	0.816
45	32	–0.07	9.98	48	0.46	9.51	0.813	32	10.48	9.44	48	12.14	7.94	0.418
40	31	–4.95	12.25	42	–3.34	11.09	0.566	31	6.37	10.34	42	8.71	9.39	0.323

Apart from CEOAEs, we evaluated otoacoustic emissions as a DP-gram function. Negley et al. [26] analyzed the DP-grams obtained using high (L_1=L_2=70 dB SPL) and moderate (L_1=65 dB SPL, L_2=50 dB SPL) intensity of stimulation, and showed that smokers presented with significantly lower DPOAE levels at all frequencies. In contrast, we used L_1=71 dB SPL and L_2 = 60 dB SPL stimulus intensities and did not document significant differences in DPOAEs levels of smokers and non-smokers on most comparisons, also when adjusted for sex. Torre et al. [35] did not find a significant effect of smoking on DPOAE levels (2.3–8.0 kHz), but their results might have been confounded by selection bias, since it included subjects who smoked no longer than for 1 year, which might be an insufficient exposure to tobacco smoke [35]. Furthermore, we showed that compared to male non-smokers, male long-term smokers presented with significantly lower DPOAE levels at 1685 Hz; this suggests a sex-specific effect of smoking on DPOAEs.

The results of our analysis of DPOAEs in an input/output function, being a highly sensitive test for the active and passive mechanisms of the cochlea, are consistent with the data published by Negley et al. [26]. These authors showed that a gradual increase

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Table 14. DPOAE levels – I/O analysis in male smokers and male non-smokers.

L2 level dB SPL	Male smokers			Male non-smokers			p	Male smokers			Male non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	1000 Hz DPOAE levels							1000 Hz SNR analysis						
70	40	9.74	5.51	31	9.83	8.57	0.956	40	12.25	5.66	31	12.63	7.85	0.814
65	43	5.76	7.02	32	8.21	5.87	0.114	43	8.38	6.74	32	11.06	7.22	0.103
60	43	4.67	7.71	29	8.33	4.62	0.025	43	7.17	7.39	29	11.76	5.33	0.005
55	41	3.60	6.08	31	5.87	8.67	0.195	41	7.77	6.16	31	9.38	8.29	0.346
50	40	1.93	6.26	30	5.32	6.36	0.029	40	6.04	6.81	30	10.01	5.25	0.010
45	36	–0.69	6.72	30	3.34	7.00	0.020	36	4.43	7.16	30	8.47	6.32	0.019
40	30	–3.44	9.07	26	1.72	6.14	0.017	30	2.15	7.46	26	6.82	6.45	0.016
	1500 Hz DPOAE levels							1500 Hz SNR analysis						
70	44	10.49	7.26	32	13.85	5.59	0.032	44	15.90	7.55	32	20.27	7.03	0.012
65	43	8.81	8.90	32	12.62	5.65	0.037	43	13.91	8.32	32	18.24	6.16	0.016
60	43	8.08	6.13	32	10.89	6.76	0.064	43	14.12	5.59	32	16.56	6.29	0.081
55	42	6.01	6.61	31	9.36	7.33	0.045	42	12.15	6.21	31	15.29	7.75	0.059
50	42	2.74	9.62	31	7.14	8.11	0.043	42	9.92	7.78	31	13.34	7.22	0.060
45	39	2.18	6.28	30	6.17	6.96	0.015	39	10.14	5.29	30	12.81	6.40	0.062
40	42	–1.66	8.57	29	1.99	10.67	0.115	42	6.31	7.80	29	9.46	9.80	0.137
	2000 Hz DPOAE levels							2000 Hz SNR analysis						
70	44	10.66	4.62	31	13.19	6.17	0.045	44	18.10	5.84	31	22.45	6.30	0.003
65	44	9.51	4.98	31	12.13	6.36	0.049	44	16.67	6.09	31	20.03	6.69	0.027
60	44	6.83	8.19	30	11.11	7.14	0.023	44	14.44	8.20	30	19.36	7.74	0.012
55	42	6.57	5.41	31	9.12	7.52	0.097	42	14.45	5.96	31	18.53	7.56	0.012
50	43	3.24	8.31	30	6.76	10.01	0.106	43	12.20	7.94	30	15.22	10.43	0.165
45	42	1.58	5.96	31	4.22	8.15	0.113	42	10.74	6.96	31	13.34	7.77	0.139
40	38	–2.09	8.18	31	–0.37	10.73	0.454	38	7.10	6.77	31	9.02	10.26	0.355
	3000 Hz DPOAE levels							3000 Hz SNR analysis						
70	43	9.85	5.04	31	11.26	7.17	0.325	43	20.00	5.28	31	21.63	7.99	0.293
65	43	8.54	6.36	31	9.72	8.91	0.509	43	17.62	6.58	31	19.43	9.88	0.349
60	44	6.68	6.55	31	8.86	6.90	0.169	44	15.82	6.91	31	18.54	6.83	0.095
55	44	4.91	7.98	32	6.89	9.75	0.335	44	14.46	7.23	32	16.47	10.11	0.315
50	44	2.78	8.99	32	5.70	7.58	0.139	44	12.78	7.71	32	15.81	7.73	0.095
45	43	–0.87	12.06	32	3.32	7.56	0.089	43	9.27	10.39	32	13.82	8.26	0.045
40	40	–3.29	12.61	30	2.34	5.53	0.025	40	8.29	10.72	30	12.83	5.94	0.041

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Table 14 continued. DPOAE levels – I/O analysis in male smokers and male non-smokers.

L2 level dB SPL	Male smokers			Male non-smokers			p	Male smokers			Male non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	4000 Hz DPOAE levels							4000 Hz SNR analysis						
70	44	13.07	6.77	30	14.84	5.11	0.228	44	22.68	6.93	30	25.95	5.40	0.033
65	44	11.84	7.18	30	13.70	5.12	0.227	44	21.05	7.24	30	23.71	4.50	0.078
60	43	10.61	7.37	31	11.23	7.24	0.720	43	19.72	7.49	31	20.81	7.77	0.547
55	42	9.20	8.56	31	9.94	7.31	0.700	42	18.21	7.96	31	18.97	7.30	0.678
50	44	6.09	9.99	31	8.09	6.64	0.333	44	16.17	9.46	31	17.69	6.83	0.445
45	43	3.41	11.15	31	5.62	7.40	0.341	43	13.21	10.03	31	15.45	7.62	0.300
40	42	0.84	11.43	32	2.76	7.67	0.415	42	10.51	10.06	32	12.48	7.47	0.356
	5000 Hz DPOAE levels							5000 Hz SNR analysis						
70	43	12.76	8.53	32	13.56	8.61	0.691	43	21.97	7.79	32	24.26	8.35	0.227
65	43	11.14	7.53	32	11.25	9.94	0.957	43	20.09	7.50	32	20.91	9.20	0.675
60	44	9.43	8.43	32	10.38	8.61	0.631	44	18.12	8.00	32	19.69	8.46	0.413
55	43	7.67	8.23	31	9.47	6.42	0.313	43	16.52	7.40	31	18.73	5.27	0.160
50	43	4.60	9.43	32	5.48	9.93	0.699	43	14.65	7.89	32	15.65	9.17	0.614
45	43	2.43	10.38	32	2.81	11.40	0.884	43	12.44	8.57	32	12.96	10.75	0.817
40	42	–1.00	11.57	31	1.00	8.67	0.421	42	9.18	9.45	31	10.94	7.08	0.387
	6000 Hz DPOAE levels							6000 Hz SNR analysis						
70	44	12.35	10.25	32	14.22	8.87	0.408	44	22.65	10.64	32	24.90	8.76	0.332
65	42	11.75	8.10	30	13.36	8.64	0.420	42	21.18	7.72	30	22.99	8.57	0.352
60	44	7.71	10.69	30	11.31	6.75	0.107	44	17.61	9.69	30	20.69	6.87	0.138
55	43	5.73	10.40	32	6.76	10.18	0.670	43	15.62	9.31	32	15.87	10.15	0.911
50	43	1.76	12.21	32	4.40	8.46	0.297	43	12.29	10.90	32	14.60	8.04	0.316
45	42	–2.10	13.28	32	–0.07	9.98	0.472	42	8.59	11.32	32	10.48	9.44	0.446
40	38	–5.92	13.34	31	–4.95	12.25	0.754	38	5.13	11.00	31	6.37	10.34	0.634

in the stimulation intensity (from 20 dB SPL to 80 dB SPL, at 10-dB intervals) is reflected by a f_2 frequency-specific increase in the I/O emission, by 10 dB, 8 dB, and 5 dB for 2 kHz, 4 kHz, and 8 kHz, respectively [26]. In our study, statistically significant differences between smokers and non-smokers were observed at 1 kHz, 1.5 kHz, 2 kHz, and 3 kHz. Moreover, we found significant differences between male smokers and male non-smokers at 1 kHz, 1.5 kHz, 2 kHz, 3 kHz, and 4 kHz, as well as between male and female smokers at 1 kHz, 2 kHz, and 5 kHz. Altogether, these findings suggest that smoking exerts particularly unfavorable effects on the cochlear OHC in men, but not in women.

Importantly, we showed that the incidence SOAEs in smokers was significantly lower than in non-smokers. This new observation requires verification in future studies.

To the best of our knowledge, our study is the first to demonstrate sex-specific differences in CEOAE, DPOAE, and OAE responses of smokers. Using an objective method for otoacoustic emission analysis, we showed that the smoking-related alterations were more pronounced in men than in women. These sex-specific differences in otoacoustic emission levels might

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Table 15. DPOAE levels – I/O analysis in female smokers and female non-smokers.

L2 level dB SPL	Female smokers			Female non-smokers			p	Female smokers			Female non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	1000 Hz DPOAE levels							1000 Hz SNR analysis						
70	42	9.03	6.38	49	9.57	5.27	0.658	42	12.13	5.53	49	13.33	5.81	0.320
65	41	8.06	6.77	49	6.73	5.83	0.320	41	10.90	4.90	49	10.73	5.57	0.880
60	41	7.69	6.69	49	6.46	5.63	0.346	41	10.54	5.75	49	10.60	6.02	0.957
55	41	6.56	6.29	46	5.13	5.94	0.279	41	10.52	5.03	46	10.12	4.60	0.695
50	39	4.66	6.75	45	2.72	8.19	0.244	39	10.01	4.94	45	8.63	8.20	0.362
45	39	2.48	7.07	42	2.40	5.44	0.952	39	7.62	5.25	42	8.41	5.54	0.513
40	34	–1.55	10.25	42	–2.25	9.33	0.757	34	4.39	8.71	42	4.77	8.11	0.844
	1500 Hz DPOAE levels							1500 Hz SNR analysis						
70	41	13.45	7.84	49	13.26	5.40	0.889	41	17.77	8.15	49	20.45	6.05	0.077
65	41	12.68	7.28	48	12.27	5.10	0.754	41	16.93	7.42	48	18.13	5.88	0.399
60	42	11.07	7.73	47	11.03	5.28	0.974	42	15.42	6.75	47	16.87	5.84	0.279
55	42	9.09	9.08	49	8.01	8.82	0.566	42	14.37	7.95	49	14.21	7.82	0.924
50	41	7.75	6.67	49	6.05	7.18	0.251	41	12.92	5.93	49	12.65	6.69	0.841
45	40	4.54	8.95	49	4.20	7.44	0.845	40	10.55	6.65	49	11.62	7.12	0.468
40	34	2.10	10.57	49	1.72	7.26	0.849	34	7.94	7.86	49	10.05	6.46	0.184
	2000 Hz DPOAE levels							2000 Hz SNR analysis						
70	42	13.20	5.72	50	11.38	5.47	0.123	42	21.49	6.43	50	20.54	6.22	0.475
65	42	12.33	5.72	50	10.68	5.44	0.160	42	19.40	5.76	50	19.42	5.81	0.988
60	42	10.60	6.06	50	9.59	5.50	0.406	42	18.10	5.87	50	18.15	6.22	0.968
55	42	8.66	6.27	50	7.68	5.50	0.425	42	16.23	6.12	50	16.72	5.63	0.691
50	41	6.70	6.31	49	5.58	5.82	0.383	41	14.96	6.06	49	14.91	5.22	0.966
45	41	4.27	6.70	49	2.03	8.98	0.192	41	12.81	5.11	49	12.19	7.80	0.659
40	38	2.19	6.70	48	–1.61	10.26	0.051	38	10.65	5.43	48	8.76	9.32	0.270
	3000 Hz DPOAE levels							3000 Hz SNR analysis						
70	42	10.54	6.11	50	10.97	4.58	0.701	42	20.90	6.41	50	22.41	4.57	0.192
65	42	9.83	6.11	50	10.07	4.50	0.833	42	19.47	5.56	50	20.05	4.29	0.572
60	42	8.20	6.24	50	8.58	5.15	0.747	42	17.40	6.10	50	18.63	5.19	0.299
55	42	7.11	6.23	50	7.41	5.22	0.803	42	16.70	6.02	50	17.67	4.78	0.394
50	42	5.15	7.00	50	5.61	5.48	0.723	42	15.05	5.48	50	15.86	4.51	0.438
45	40	1.53	10.80	50	2.46	7.84	0.637	40	11.67	8.74	50	13.73	7.21	0.224
40	39	1.38	6.45	50	–0.37	8.02	0.270	39	11.89	5.03	50	10.95	7.13	0.484

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Table 15 continued. DPOAE levels – I/O analysis in female smokers and female non-smokers.

L2 level dB SPL	Female smokers			Female non-smokers			p	Female smokers			Female non-smokers			p
	n	mean	SD	n	mean	SD		n	mean	SD	n	mean	SD	
	4000 Hz DPOAE levels							4000 Hz SNR analysis						
70	42	14.44	5.75	50	14.11	5.26	0.771	42	24.79	6.36	50	25.26	5.52	0.707
65	42	13.52	5.85	50	13.22	5.08	0.794	42	22.70	6.01	50	23.53	5.37	0.483
60	42	11.90	6.24	50	11.87	5.15	0.974	42	22.03	5.72	50	22.00	5.21	0.980
55	42	10.61	6.60	50	10.43	5.56	0.889	42	20.50	6.15	50	20.79	5.02	0.805
50	42	8.40	8.75	50	8.61	5.54	0.886	42	18.37	7.55	50	19.18	4.98	0.540
45	42	5.55	9.59	50	5.89	7.59	0.850	42	15.65	7.75	50	16.58	6.54	0.537
40	42	2.67	10.59	48	4.14	6.17	0.414	42	12.62	8.85	48	14.55	5.84	0.220
	5000 Hz DPOAE levels							5000 Hz SNR analysis						
70	42	15.52	7.48	50	14.77	6.51	0.611	42	25.57	6.95	50	25.47	6.35	0.942
65	42	13.63	7.49	50	12.62	7.27	0.513	42	22.58	6.69	50	22.38	6.20	0.883
60	42	12.35	7.21	50	11.14	8.86	0.478	42	21.80	6.58	50	21.18	7.87	0.688
55	42	9.92	7.66	50	9.45	7.64	0.770	42	19.66	6.22	50	19.41	6.31	0.848
50	41	7.44	9.21	50	7.10	8.19	0.853	41	17.00	7.20	50	17.11	7.03	0.942
45	42	4.03	10.65	50	5.42	8.20	0.480	42	14.50	8.44	50	15.84	6.67	0.397
40	41	0.66	12.41	49	3.36	6.92	0.196	41	10.76	10.43	49	13.62	6.50	0.117
	6000 Hz DPOAE levels							6000 Hz SNR analysis						
70	42	14.84	8.32	50	13.93	6.97	0.573	42	25.40	7.74	50	25.19	7.20	0.894
65	42	12.69	8.41	50	12.04	6.98	0.683	42	22.36	7.74	50	22.22	6.65	0.921
60	42	10.40	9.16	50	9.35	7.83	0.557	42	20.28	7.49	50	19.56	7.13	0.638
55	40	7.59	11.66	49	6.91	7.27	0.735	40	18.03	9.68	49	17.64	6.23	0.821
50	41	2.99	14.27	49	3.75	8.90	0.759	41	13.30	12.07	49	15.01	7.14	0.406
45	39	1.59	12.31	48	0.46	9.51	0.629	39	11.55	9.94	48	12.14	7.94	0.760
40	40	–2.75	13.34	42	–3.34	11.09	0.828	40	8.09	10.74	42	8.71	9.39	0.781

reflect the influence of genetic, hormonal, behavioral, and/or environmental factors.

Previous studies documented evident sex-specific differences in the CEOAE levels of infants and children. Cassidy and Ditty [36] showed that compared to male newborns, female newborns present with significantly higher CEOAE levels at 1.6 kHz, 2.4 kHz, 3.2 kHz, and 4.0 kHz. Also, Aidan et al. [37] demonstrated that mean CEOAE levels in female neonates are higher than in male neonates (22.1 dB SPL *vs.* 21.4 dB SPL). Interestingly, the same study documented significant differences in the CEOAE levels recorded in the right and left ear (22.4 dB SPL *vs.* 21 dB SPL) [37]. In another study, 12-year-old girls were shown to present with significantly higher CEOAE levels than their male peers [38]. However, in contrast to Aidan et al. [37], the authors of this study did not observe a bilateral asymmetry in CEOAE levels [38]. Although we did not reveal sex-specific differences in the otoacoustic emission levels of non-smokers, it cannot be excluded that men present with a genetically determined (i.e., sex hormone-independent) greater susceptibility of cochlear OHCs to the ototoxic components of tobacco smoke.

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The results of experimental studies point to a potential protective effect of female sex hormones as an explanation of sex-specific differences in hearing. Estrogens, 17α-estradiol, 17β-estradiol, estrone, and estriol were shown to protect against gentamicin-induced outer hair cell death; the effect of 17β-estradiol is mediated by estrogen receptor (ER) [39]. Interestingly, the expression of estrogen receptors ERα and ERβ in the inner ear (i.e., in the nuclei of stria vascularis, outer and inner hair cells, spiral ganglion cells, vestibular ganglion cells, and vestibular dark cells) is known to decrease with age [40]. These findings are consistent with the results of clinical studies. For example, Kilicdag et al. [21] demonstrated that estrogen therapy may protect against hearing loss in aging postmenopausal women. Taking this evidence into account, it can be hypothesized that female sex hormones may also protect against tobacco smoke-induced hearing impairment.

Behavioral factors should also be considered as a potential cause of sex-specific differences in susceptibility to tobacco smoke-related hearing loss. Men not only smoke more, but also use stronger cigarettes, as well as other stimulants [41–43]. Our study included 21 women and 22 men, who smoked at least 15 cigarettes per day for at least 7 years. We did not compare, however, the total number of cigarettes smoked by the female and male participants. Consequently, our male smokers might be exposed to tobacco smoke more often and for a longer period of time than female smokers. Finally, the influence of environmental chemical ototoxins should be taken into account as a confounding factor resulting in greater impairment of hearing in our male smokers [44].

To summarize, tobacco smoke likely induces an array of subclinical changes in the organ of hearing, especially in males. Therefore, appropriate strategies preventing resultant hearing loss should be implemented before it will manifest clinically and impair patient functioning. These strategies should be adjusted for these documented sex-specific differences in susceptibility to tobacco smoke-induced hearing impairment.

Conclusions

This study showed that smoking induces an array of subclinical changes in the organ of hearing. Specifically, while it does not modulate the hearing threshold determined with PTA at low, moderate, and high frequencies, it causes a significant decrease in OAE levels, but only in males. Furthermore, smoking impairs the active and passive mechanisms of male cochlea.

Disclaimers

No conflicts of interest to be noted. No relationships with industry to be noted.

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