

Relating tinnitus features and audiometric characteristics in a cohort of 34 tinnitus subjects

María Cuesta, Pedro Cobo

Institute of Physical and Information Technologies (ITEFI), CSIC, Serrano 144, 28006 Madrid, Spain
m.cuesta@csic.es ORCID: <http://orcid.org/0000-0002-7729-8568>
pedro.cobo@csic.es ORCID: <http://orcid.org/0000-0002-3406-1122>

Submitted: 08/11/2017. Accepted 03/05/2018. Publicado online: 10/01/2019

Citation / Cómo citar este artículo: María Cuesta and Pedro Cobo. (2018). *Relating tinnitus features and audiometric characteristics in a cohort of 34 tinnitus subjects*. *Loquens*, 5(2), e054. <https://doi.org/10.3989/loquens.2018.054>

ABSTRACT: Although tinnitus, the conscious perception of a sound without a sound source external or internal to the body, is highly correlated with hearing loss, the precise nature of such correlation remains still unknown. People with high pitch tinnitus are used to suffer from high frequency hearing losses, and vice versa, low pitch tinnitus is mostly associated with low frequency hearing losses. However, many subjects with low or high frequency losses do not develop tinnitus. Thus, studies trying to relate audiometric characteristics and tinnitus features are still relevant. This article presents a correlational study of audiometric and tinnitus variables in a sample of 34 subjects, paying special attention to the heterogeneous subtypes of both audiometry shape and tinnitus etiology. Our results, which concur with others previously published, demonstrate that the tinnitus pitch, the main frequency of the tinnitus spectrum, in subjects with high-steep high-frequency and continuously steep hearing losses, are highly correlated with the frequency at which hearing loss reaches 50 dB HL.

Keywords: hearing loss; tinnitus; audiometry; tinnitus pitch.

RESUMEN: *Relación entre las características audiométricas y acufenométricas en un grupo de 34 pacientes de acúfeno.*— Aunque el acúfeno, la percepción consciente de un sonido en ausencia de una fuente externa o interna, está altamente correlacionada con las pérdidas auditivas, aún no se conoce la naturaleza precisa de esta relación. Las personas con acúfeno de alta frecuencia suelen tener pérdidas auditivas de alta frecuencia, y viceversa, cuando el acúfeno percibido es de baja frecuencia, las pérdidas auditivas también afectan a la parte de baja frecuencia del espectro auditivo. Sin embargo, hay muchas personas que sufren de pérdida de audición y sin embargo no desarrollan el acúfeno. Por consiguiente, aún son pertinentes los estudios que tratan de relacionar características audiométricas y acufenométricas en una misma muestra de sujetos. Este artículo presenta los resultados de un estudio correlacional en una muestra de 34 participantes, prestando especial atención a los distintos y heterogéneos subtipos tanto de audiometría como de etiología del acúfeno. Nuestros resultados, que están de acuerdo con otros publicados previamente, demuestran que la frecuencia del acúfeno, en los subtipos de audiometría con una pendiente alta en alta frecuencia y en estos con una pendiente continuamente decreciente, está altamente correlacionada con la frecuencia a la cual la pérdida de audición alcanza los 50 dB HL.

Palabras clave: pérdida auditiva; acúfeno; audiometría; frecuencia del acúfeno.

1. INTRODUCTION

Tinnitus is the conscious perception of sound heard in the absence of physical sound sources external or internal to the body (Eggermont & Tass, 2015). Epidemiological studies report that tinnitus roughly

affects 10% of the adult population (Hall et al., 2015) and severely disturbs the quality of life of about 1–2% of adults by producing anxiety, annoyance, irritability, disturbed sleep patterns, and depression (Cobo, 2015; Diges, Simón, & Cobo, 2017; Van de Heyning et al., 2007; Vio & Holme, 2005).

Similar to in phantom limb pain, tinnitus perception seems to be the correlate of maladaptive attempts of the brain at reorganization due to deprived sensory input. Therefore, hearing loss (HL) is the most important risk factor for developing tinnitus (Kleinjung, Steffens, Struz, & Langguth, 2009). The central auditory system compensates for diminished input by upregulating its responsiveness in central circuitries. Central compensation that follows reduced auditory nerve activity may occur first at the level of the auditory brainstem, from where altered activity patterns then spread to ascending auditory nuclei. Electrophysiological and functional imaging measurements in humans and animals suggest the following neural correlates of tinnitus in the auditory system (Eggermont, 2012):

- Increased neural synchrony (hypersynchrony)
- Increased spontaneous firing rates (hyperactivity)
- Reorganization of tonotopic map

Tinnitus can occur at both sub-cortical and/or cortical levels, suggesting two different tinnitus subtypes: cochlear and central (Noreña, 2011; Milloy, Fournier, Benoit, Noreña, & Koravand, 2017). Cochlear tinnitus results from a hyperactivity at the acoustic nerve and is the subtype taking place in salicylate induced tinnitus in animal models. Central tinnitus, on the other hand, outcomes due to cortical changes (mainly hypersynchrony and tonotopic map reorganization) due to HL, and is the subtype happening in noise induced tinnitus in animal models (Noreña, 2011).

Tinnitus and HL are highly correlated. According to Eggermont (2014), the prevalence of tinnitus is a cubic-root function of the prevalence of significant HL (HL > 25 dB from 500 Hz to 4 kHz). However, although chronic tinnitus is often accompanied by some kind of hearing deficit, it is still unknown how HL can actually produce tinnitus, as many HL impaired people do not develop tinnitus. The intriguing relationship between tinnitus and HL is even more disconcerting as 25% of tinnitus participants in a research study had normal hearing up to 8 kHz (Roberts, Moffat, & Bosnyak, 2006).

Many researchers have investigated how the tinnitus occurrence and the HL curve (the audiogram) shape are related (König, Schaette, Kempster, & Gross, 2006; Langguth et al., 2017; Schecklmann et al., 2012; Sereda et al., 2011; Shekhawat, Searchfield, & Stinea, 2014). For example, the perceived frequency of tinnitus, also called the tinnitus pitch (TP in the following), is usually associated with frequencies showing HL, i.e., high pitch tinnitus is associated to high frequencies HL, and low pitch tinnitus with low frequencies HL (Shekhawat et al., 2014).

Different theories have been proposed to relate different types of HL with TP (Schecklmann et al., 2012). Roberts, Bosnyak, Bruce, Gander, and Paul (2015), based in similarity judgments, reported that tinnitus subjects matched their TP near the edge frequency of the audiogram, that is, the frequency at which the HL commences. Thus, one theory proposes the edge frequency as

the mechanism triggering the tinnitus by a lateral inhibition imbalance, which results in an over representation of this edge frequency at cortical level (reorganization of the tonotopic map). According to this theory, the TP should correspond to the edge frequency of the HL.

Shekhawat et al. (2014) proposed the frequency associated to dead region as the most likely audiometric characteristic related to TP. Previously, Weisz, Hartmann, Dohrmann, Schlee, and Noreña (2006) demonstrated that 72.7% of tinnitus sufferers had dead regions. The dead region is the cochlea zone where the inner ear cells (IHC) are not functioning. In fact, IHC damage has been identified as a prerequisite for auditory pathway deafferentation and tonotopic reorganization. Post mortem studies have demonstrated that IHC damage starts roughly at HL = 50 dB (Shekhawat et al., 2014). Therefore, the frequency at which HL = 50 dB (F50 in the following) was proposed by Shekhawat et al. (2014) as the most probable audiometric correlate of TP. Other possible audiometric correlates of TP were analyzed by Shekhawat et al. (2014), namely, the frequency at which HL approximately begins, that is the frequency for HL = 20 dB (F20 in the following), and the frequency at which HL is maximum (Fmax in the following). Notice that F20 could be assimilated to the edge frequency proposed by Roberts et al. (2015).

Alternatively, Schecklmann et al. (2012) suggested that tinnitus is caused by homeostatic plasticity, which compensates for deprived sensory input by increasing spontaneous firing rate and neural synchrony in the corresponding auditory pathway. According to this theory, the TP should correspond to the frequency for maximum HL, that is, Fmax.

Therefore, studies of relationship between audiometric characteristics, obtained from the HL curve shape, and tinnitus features, mainly the TP, are still relevant. Hence, the aim of this article is to provide the results of such a study in a cohort of 34 tinnitus volunteers, which undertook joint audiometric and tinnitus measurements in our laboratory. When analyzing the relationship between tinnitus features and audiometric characteristics, the following issues should be taken into consideration:

1. The procedure to assess the tinnitus features, for instance, the tinnitus pitch.
2. The way the audiometric characteristics are obtained, namely, which attributes from the HL are used and how they are measured.
3. The statistical methods used for testing tinnitus features and audiometric characteristics.

2. MATERIAL AND METHODS

2.1. Participants

The study was approved by the Research Bioethics Subcommittee of the Spanish National Research Council (CSIC) and was conducted in accordance with the Spanish

Law of Data Protection (RD1720/2007). 34 volunteers with tinnitus (21 men, age 51±14 years, 13 women, age 45±11 years) were recruited through Spanish Tinnitus Associations and Tinnitus Clinics. Subjects with audiological surgical history (otosclerosis, tumors, head trauma...) were excluded. All participants in this study gave their written informed consent.

Columns 1–3 of Table 1 show the assigned number, sex and age, respectively, of each participant.

2.2. Audiometric measurements

Each subject underwent HL measurements by pure-tone audiometry of both ears. HL curves were measured with the Clinic Audiometer GSI 60, using pure tones at 11 pre-specified frequencies (125, 250, 500 750, 1000, 1500, 2000, 3000, 4000, 6000, and 8000 Hz). 32 of 35 subjects have HL similar for left and right ears. On the other hand, 3 of 35 (18, 21, and 25) have HL_{left ear} and

Table 1: Audiometric characteristics of participants.

Subject	Sex	Age	HL subtype	F20 _{left ear}	F20 _{right ear}	F50 _{left ear}	F50 _{right ear}	Fmax _{left ear}	Fmax _{right ear}
			(*)	(Hz)	(Hz)	(Hz)	(Hz)	(Hz)	(Hz)
1	F	45	F	n/a	n/a	n/a	n/a	125	125
2	M	63	HS	1498	1928	2599	1499	8000	8000
3	M	39	F	499	748	n/a	n/a	1500	750
4	M	44	HS	4665	4996	5998	9000	6000	8000
5	M	53	HS	2498	2496	3998	7980	8000	8000
6	M	50	HS	3496	998	7712	9000	8000	8000
7	M	43	HS	3664	6796	9000	9000	8000	8000
8	F	50	HS	6661	249	9000	9000	8000	8000
9	F	41	CS	167	208	500	749	6000	8000
10	F	67	HS	249	4496	9000	9000	6000	8000
11	M	28	F	n/a	n/a	n/a	n/a	6000	6000
13	F	45	CS	125	125	9000	2995	750	8000
14	M	62	HS	417	437	3363	2666	6000	6000
15	M	31	ST	1083	750	1624	1278	2000	2000
16	M	68	CS	499	624	5997	7996	8000	8000
17	F	47	HS	1498	4748	5330	6000	6000	6000
18	M	65	HS	125	1498	999	9000	8000	8000
19	F	61	F	749	5991	n/a	n/a	1000	8000
20	M	41	F	6991	n/a	n/a	n/a	8000	125
21	M	47	ST	2398	2332	3500	3249	3000	4000
22	F	45	CS	156	125	2798	3495	4000	6000
23	M	42	F	2498	2996	n/a	n/a	3000	3000
24	M	37	F	3998	7981	n/a	n/a	6000	8000
25	M	69	HS	498	249	1999	7197	6000	8000
26	M	44	F	5991	n/a	n/a	n/a	6000	6000
27	F	26	F	n/a	n/a	n/a	n/a	6000	8000
28	F	29	ST	3997	3331	5000	5000	6000	4000
29	M	58	HS	1996	2331	5327	6796	8000	8000
30	F	42	F	333	n/a	n/a	n/a	6000	125
31	F	41	F	5994	n/a	n/a	n/a	6000	8000
32	M	36	HS	2499	2428	4990	6000	6000	6000
33	M	75	HS	125	125	1374	2444	6000	8000
34	F	50	HS	2331	1998	7994	5994	8000	6000

(*) F=Flat, HS=High-steep high-frequency, CS=Continuously steep, ST= Scotoma

Figure 1: Mean HL (superimposed to individual HL) for flat HL subtype and (a) right ear, (b) left ear.

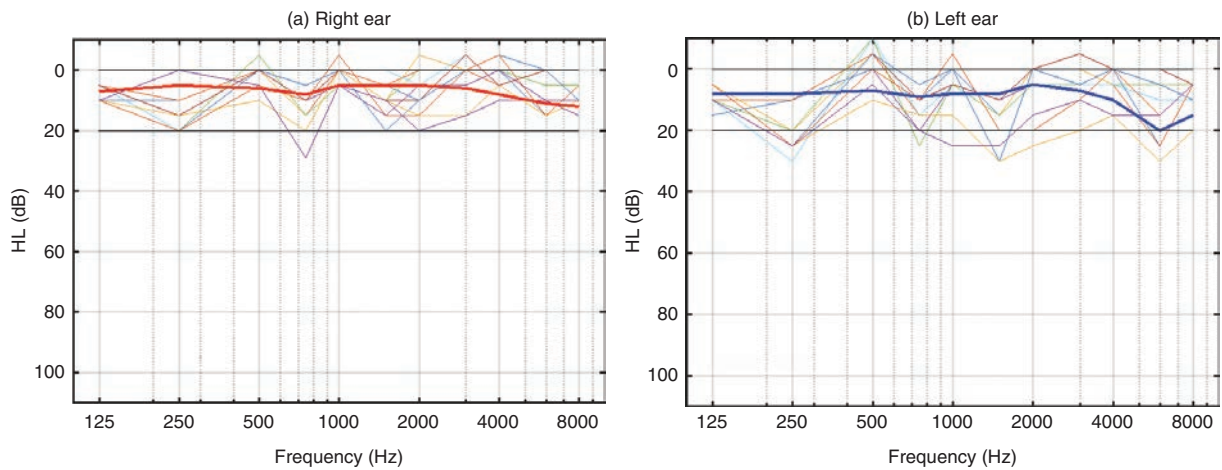
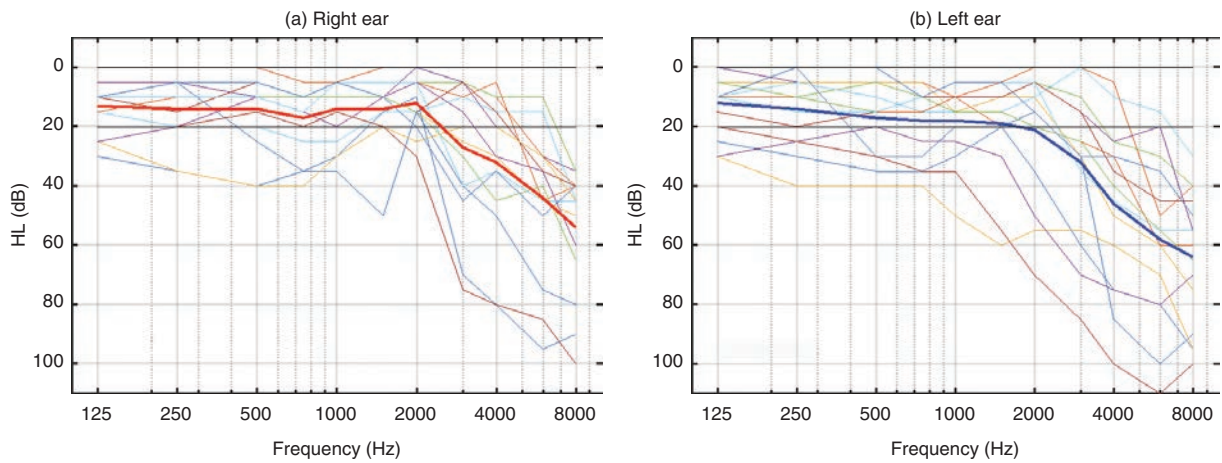


Figure 2: Mean HL (superimposed to individual HL) for high-steep high-frequency HL subtype and (a) right ear, (b) left ear.



$HL_{right\ ear}$ significantly different. Looking at the HL curves of participants, four subtypes can be defined:

1. Roughly flat HL (Figure 1; participants 1, 3, 11, 19, 20, 23, 24, 26, 27, 30, and 31).
2. High-steep high-frequency HL (Figure 2) (participants 2, 4, 5, 6, 7, 8, 10, 14, 17, 18 (left ear), 25 (more in left ear), 29, 32, 33, and 34).
3. Continuously steep HL (Figure 3; participants 9, 12, 13, 16, and 22).
4. HL with a scotoma (Figure 4; participants 15, 21, and 28).

Figures 1–4 depict mean HL curves (superimposed to individual HL) for these four subtypes. Column 4 of Table 1 shows the HL subtype of each participant.

2.3. Audiometric characteristics

The frequencies at which HL attains 20 dB, F20, 50 dB, F50, and its maximum, Fmax, for left and right ears, are summarized in Table 2. To improve the estimation of F20

and F50, finer HLs are linearly interpolated first from measured HLs. This interpolation improves the estimation of the cutting of HL curves with HL = 20 and HL = 50. However, despite this interpolation, it was not possible to find F20 and F50 for some cases (mainly for flat HL subtypes), as HL curves do not reach these values. In these cases, n/a is used for the corresponding F20 and F50 values. The HL curves of some participants deserve special consideration. Firstly, HLs are greater than 20 dB for subject 13, in both ears, and for subject 18, in left ear. In these cases, we assign arbitrarily F20 = 125 Hz. Secondly, HL < 50 in subjects 6, 7, 8, 10, 13, 18, 21, 28, and 32. In these subjects, F50 are assigned to the closer frequency at which HL = 40 or 45 dB.

2.4. Tinnitus features

The tinnitus characteristics were assessed on the basis of the responses of the participants to the clinical evaluation sheet. The interview to participants included temporal (variability), spectral (pitch), and spatial (location) aspects of their tinnitus. Furthermore, additional information of

Figure 3: Mean HL (superimposed to individual HL) for continuously steep HL subtype and (a) right ear, (b) left ear.

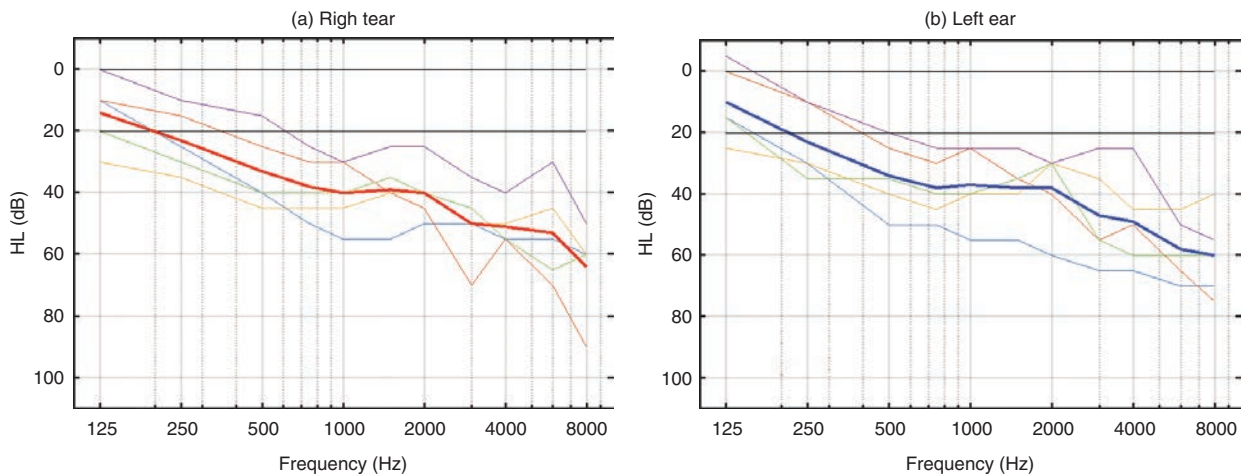
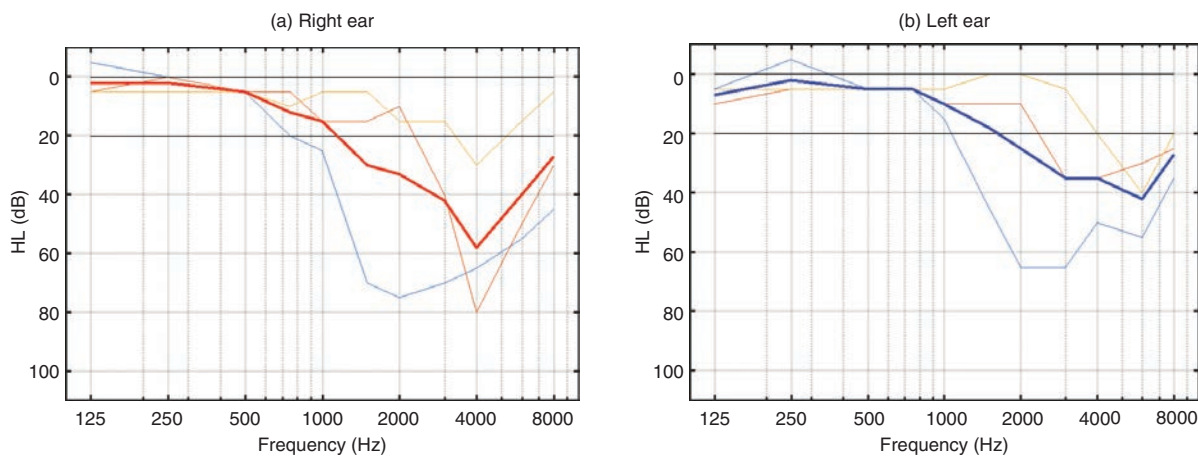


Figure 4: Mean HL (superimposed to individual HL) for HL with scotoma subtype and (a) right ear, (b) left ear.



participants was obtained, including anamnesis (clinic history), tinnitus severity through Visual Analog Scale (VAS) and a Spanish version of the Tinnitus Handicap Inventory (THI; Herráiz, Hernández Calvín, Plaza, Tapia, & de los Santos, 2001). The anamnesis included information about the history and descriptive characteristics of the tinnitus, their possible etiology, previous tinnitus treatments, and relevant comorbidities.

The type and pitch of the tinnitus were evaluated using the self designed Graphical User Interface (GUI) of Figure 5. Using this GUI, tones, ringing and hissing sounds can be easily generated. This is accomplished by creating a band-pass filtered noise. Two parameters (central frequency and bandwidth) determine the type of sound. The bandwidth is defined as a percentage of the central frequency. For instance, for tones the band-pass is very narrow (0.1%). Ringing are narrowband noises (bandwidth lesser than 10%) while hissing are wideband noises (bandwidth greater than 10%).

For tinnitus pitch matching, participants were sat in front of the computer where the GUI runs. Firstly, they

are trained in how tones, ringing, and hissing sound. Then, they are asked to identify roughly which sound is more similar to their tinnitus. After that, subjects are trained on the effect of central frequency and bandwidth on the sounds. Finally, a bracketing procedure is used to match as close as possible the sound generated by the GUI to its own tinnitus. It must be mentioned that some participants referred several types of sounds. In this case, the GUI is run consecutively to match all the sounds perceived by the participant.

Table 3 summarizes the resulting tinnitus characteristics of participants. Tinnitus is located either to left ear, right ear, bilateral (both ears), or the centre head. Some participants hear different types of tinnitus in each ear. A variety of etiologies were identified by the subjects, including sensorineural HL, conductive HL (otitis, Eustachian tube dysfunction), stress, noise, head trauma, and sinusitis. Some of the participants referred several possible origins of their tinnitus. When a tinnitus trigger is not clearly identified, the etiology is referred as idiopathic.

2.5. Data analysis

Numerical proportions of different types of HL and tinnitus are appraised first by pie charts. Then, scatter plots and Spearman rank correlation analysis are applied

Table 2: Comparison of F20, F50, Fmax, and TP for the different HL subtypes.

HL subtype	Subject	F20 (Hz)	F50 (Hz)	Fmax (Hz)	TP (Hz)
HS	2	1748	2049	8000	5000
	4	4830	7500	7000	4500
	5	2498	3998	8000	4400
	6	3496	712	8000	12500
	7	3664	9000	8000	7000
	8	3455	9000	8000	8000
	10	249	9000	6000	5000
	14	437	2666	6000	3100
	17	1498	5330	6000	5200
	18	811	5000	8000	3900
	25	498	1999	6000	3500
	29	1996	5327	8000	5500
	32	2499	4990	6000	3100
	33	125	1909	7000	3500
34	2165	6994	7000	7500	
CS	9	167	500	6000	3000
	12	416	2664	8000	4000
	13	125	5997	750	3800
	16	561	6998	8000	8300
	22	145	3145	5000	2000
ST	15	917	1451	2000	2400
	21	2332	3249	3000	12000
	28	3664	5000	5000	3000

to paired tinnitus and audiological variables. Spearman rank correlation is used to identify and test the strength of relationships between these variables (Diges, Simón, & Cobo, 2017). Positive Spearman correlation coefficients (ρ) between x and y variables denote that both variables increase monotonically, and vice versa, a negative correlation coefficient indicates that when x increases y decreases monotonically. The correlation between the variables is considered to be very weak for $|\rho| \leq 0.2$, weak for $0.2 < |\rho| \leq 0.4$, moderate for $0.4 < |\rho| \leq 0.6$, strong for $0.6 < |\rho| \leq 0.8$, and very strong for $|\rho| > 0.8$.

3. RESULTS

Numerical proportion analysis of each HL subtype (Figure 6) show that 44% (15 of 34) of the participants have HL curves roughly flat at low frequencies and high steep at high frequencies; 32% (11 of 34) of the participants have more or less flat HLs. HLs are continuously steep for 15% (5 of 34) of participants. And, for the other 9% (3 of 34), HLs have a scotoma at 4–6 kHz.

Numerical proportional analysis applied to tinnitus laterality, tinnitus sound, and tinnitus etiology, of 23 subjects of HS, CS, and ST HL subtypes, affords the results depicted in Figure 7. Concerning the tinnitus laterality, Figure 7a, 43% of subjects (10 of 23) allocate their tinnitus to left ear, in 35% of subjects (8 of 23) the tinnitus is bilateral, 13% (3 of 23) perceive the tinnitus in the head (central), and only 2 of 23 (8%) assign their tinnitus to the right ear. Notice that there are people with several types of tinnitus, allocated to distinct parts of the head. In these cases, tinnitus is assigned to the dominant (more intense) tinnitus. Regarding the tinnitus sound, Figure 7b, the more frequent is tonal (39%, 9 of 23), followed by ringing (35%, 8 of 23), and hissing (26%, 6 of 23). As before, when subjects refer to several tinnitus sounds, the more prominent is assigned. Finally, the predominant tinnitus etiology (Figure 7c) was sensorineural HL (HL induced in Table 3), with a percentage of 39% (9 of 23), followed by noise (30%, 7 of 23), idiopathic (13%,

Figure 5: MATLAB GUI for tinnitus pitch matching.

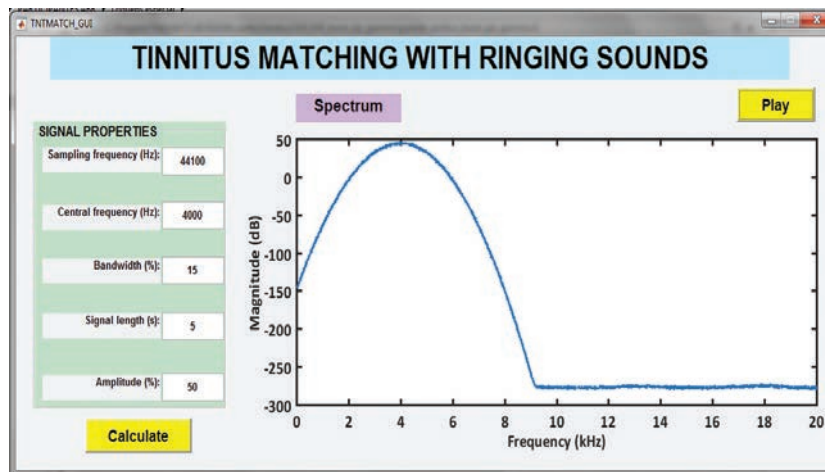


Table 3: Tinnitus features of participants.

<i>Subject</i>	<i>Sex</i>	<i>Age</i>	<i>Tinnitus duration (years)</i>	<i>Tinnitus location</i>	<i>Tinnitus sound</i>	<i>Tinnitus pitch (Hz)</i>	<i>Tinnitus bandwidth (%)</i>	<i>THI</i>	<i>VAS</i>	<i>Tinnitus Etiology</i>
1	F	45	0.7	Bilateral	Ringling	2200	1	60	75	Idiopathic
2	M	63	10	Bilateral	Hissing	5000	30	4	30	HL induced
3	M	39	2	Left ear	Tonal	6000		16	55	Idiopathic
4	M	44	2.8	Central	Ringling	4500	1	74	75	HL induced
5	M	53	4	Left ear	Ringling	4400	4	10	15	Stress. HL induced
6	M	50	7	Left ear	Tonal	12500		20	25	HL induced
7	M	43	3	Left ear	Ringling	7000	3	34	65	Idiopathic
8	F	50	10	Bilateral	Tonal	8000		22	30	Head trauma induced
9	F	41	14	Left ear	Tonal	3000		38	55	HL induced
10	F	67	1	Left ear	Tonal	4000		36	75	Idiopathic etiology
					Ringling	6000	5			
11	M	28	14	Bilateral	Tonal	9000		42	60	Head trauma induced
12	M	72	11	Left ear	Tonal	4000		54	50	Noise induced
13	F	45	8	Bilateral	Tonal	3800	1	64	70	Idiopathic
					Ringling	250				
14	M	62	10	Right ear	Ringling	3100	1	18	65	HL induced
15	M	31	0.3	Bilateral	Hissing	2400	17	88	85	Noise induced
16	M	68	16	Bilateral	Tonal	8300		30	75	Stress. HL induced
17	F	47	12	Left ear	Tonal	5200		50	75	Eustachian tube dysfunction
18	M	65	20	Bilateral	Ringling	300 (RE)	5	52	70	Otitis. HL induced
						7000(LE)	7			
19	F	61	0.4	Left ear	Hissing	1000	25	14	25	Noise induced
20	M	41	1	Left ear	Ringling	8000	1	50	60	Idiopathic
21	M	47	8	Right ear	Ringling	12000	5	10	55	Noise induced
22	F	45	0.3	Central	Hissing	100	60	56	55	HL induced
						2000	50			
23	M	42	0.1	Left ear	Ringling	7000	10	36	65	Otitis
					Tonal	7000				
24	M	37	1.1	Left ear	Ringling	7000	2	26	30	Eustachian tube dysfunction
25	M	69	0.8	Left ear	Hissing	3500	20	48	60	Stress. Noise induced
26	M	44	1.3	Left ear	Tonal	8800		62	70	Stress. Idiopathic
27	F	26	0.17	Central	Hissing	1500	20	62	70	Stress. Eustachian tube dysfunction
					Tonal	8000				
28	F	29	0.25	Bilateral	Hissing	3000	20	96	75	Stress. Acoustic trauma.
29	M	58	0.25	Left ear	Tonal	5500		22	35	HL induced
30	F	42	0.42	Bilateral	Hissing	125 (LE)	20	32	55	Stress.
					Tonal	4000 (RE)				
						9000 (RE)				
31	F	41	1.3	Left ear	Hissing	1000	40	70	70	Stress. Sinusitis. Eustachian tube dysfunction
32	M	36	0.33	Left ear	Tonal	3100		50 (day) 80(night)	82	Head trauma. Noise induced
33	M	75	0.25	Central	Hissing	4000	30	80	84	Noise induced
					Tonal	3500				
34	F	50	1.5	Bilateral	Tonal	7500		65	76	HL induced

3 of 23), conductive HL (9%, 2 of 23), and head trauma (9%, 2 of 23). Notice that stress (see Table 3) was considered a comorbid effect and not a triggering cause of tinnitus.

Table 2 summarizes the mean F20, F50, and Fmax for the participants with HS, CS, and ST subtypes, together with the corresponding tinnitus pitches. For subjects with

unilateral tinnitus, the F20, F50, and Fmax values of the corresponding ear are chosen. For subjects with either bilateral or central tinnitus, the mean of left and right ears is selected.

Figure 8 shows the mean differences between TP and F20, TP and F50, and TP and Fmax. For HS HF and CS HL subtypes, it can be seen that F20 underestimates, Fmax overestimates, and F50 is the closest estimator of the TP. For ST HL subtype, the three variables underestimate the tinnitus pitch. Figure 9 shows the average HL curves for the three HL subtypes with the values of F20, F50, Fmax, and TP superimposed.

Figures 10–12 show scatter plots for F20 versus TP, F50 versus TP, and Fmax versus TP, for the three HL subtypes, respectively. Again, for the HS and CS subtypes, it can be seen that F20 underestimates TP, Fmax overestimates TP, and F50 is the best estimator of TP. For HL curves with scotoma, neither F20, F50 nor Fmax approach sufficiently to TP. However, taking into account that ST subgroup has only three participants, this assertion does not have enough statistical power. Since scatter results are similar for HS and CS HL subtypes, we could integrate both in just a subgroup. Figure 13 shows a joint scatter plot for both subtypes. Table 4 summarizes the ρ and p values obtained when applying Spearman rank correlation to the paired variables F20-TP, F50-TP, and Fmax-TP for the join HS

Figure 6: HL curves subtypes.

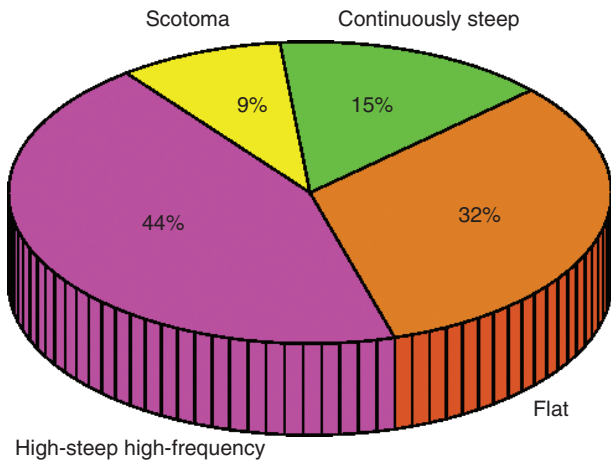


Figure 7: (a) Tinnitus laterality, (b) Tinnitus sound, and (c) Tinnitus etiology.

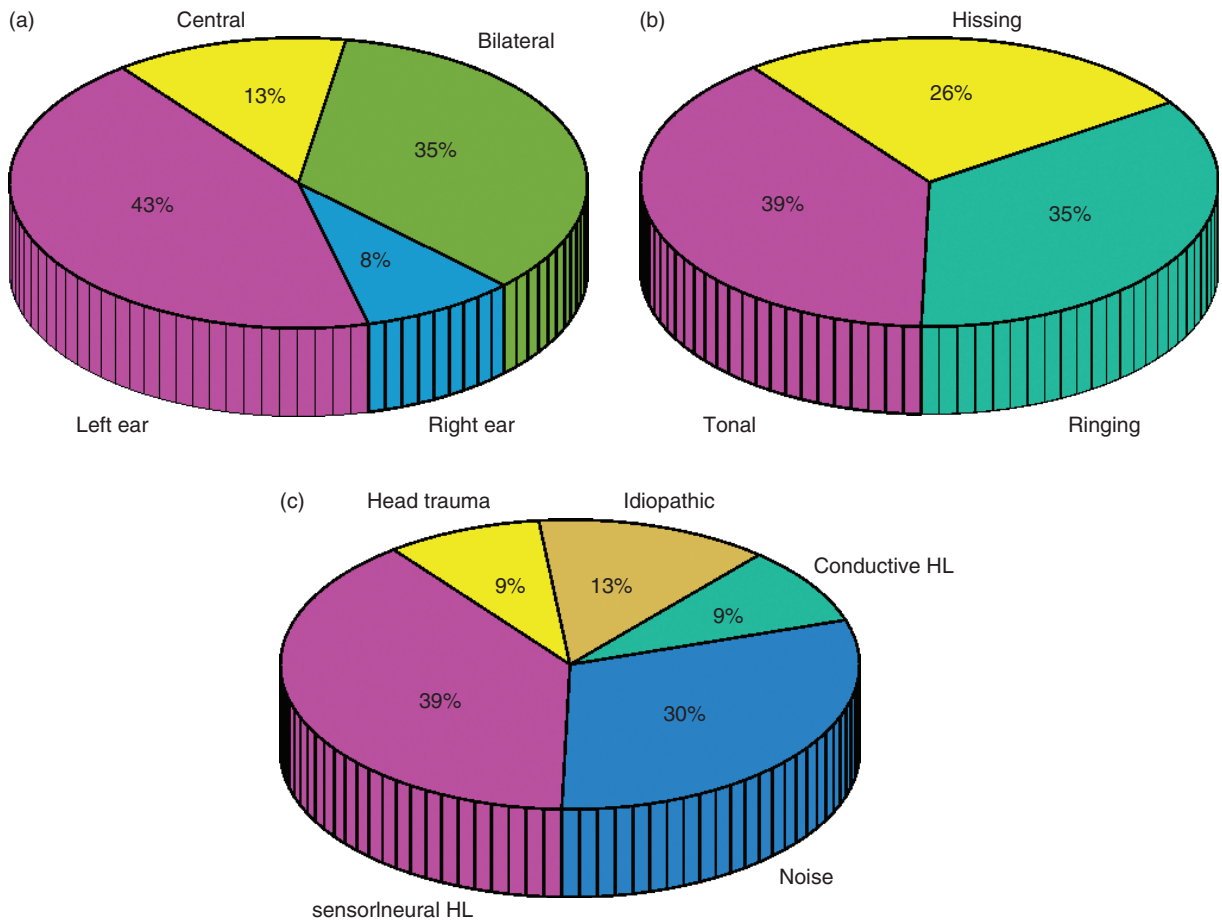


Figure 8: Mean differences between TP and F20, F50 and Fmax for (a) high-steep high-frequency HL subtype, (b) continuously steep HL subtype, and (c) HL with scotoma subtype.

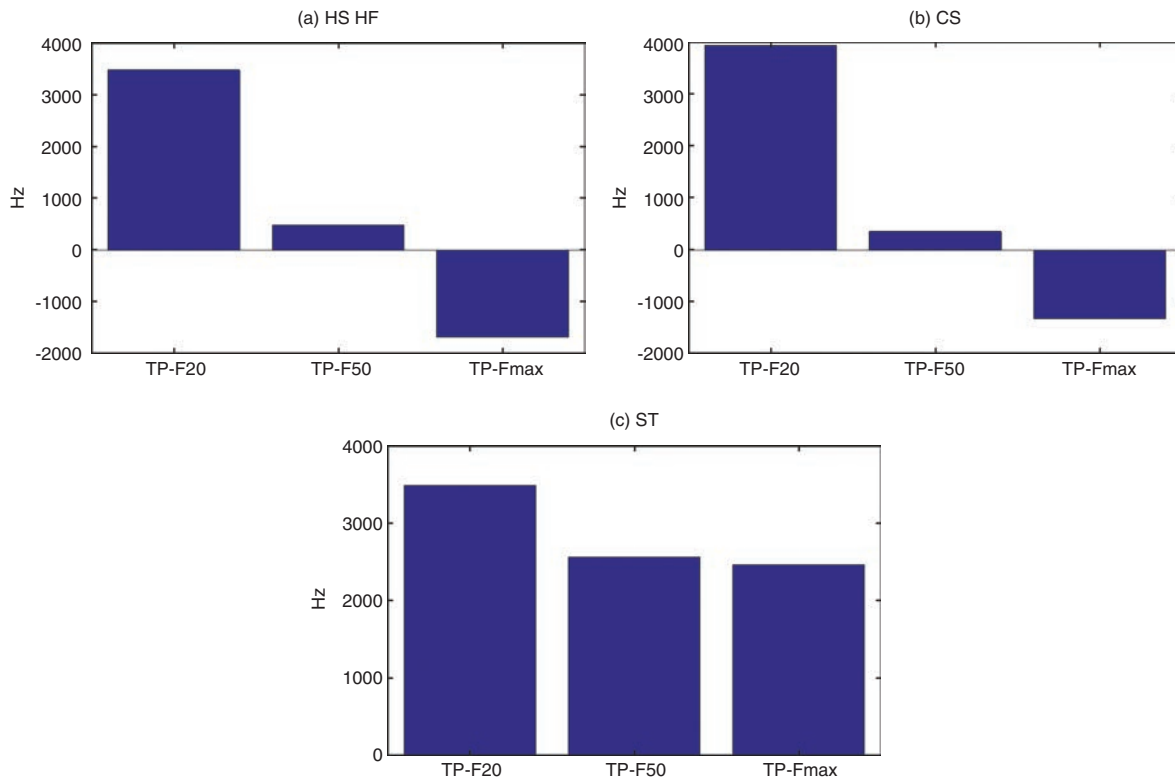


Figure 9: Mean HL curves for the three subtypes, with the values of F20, F50, Fmax, and TP overimposed.

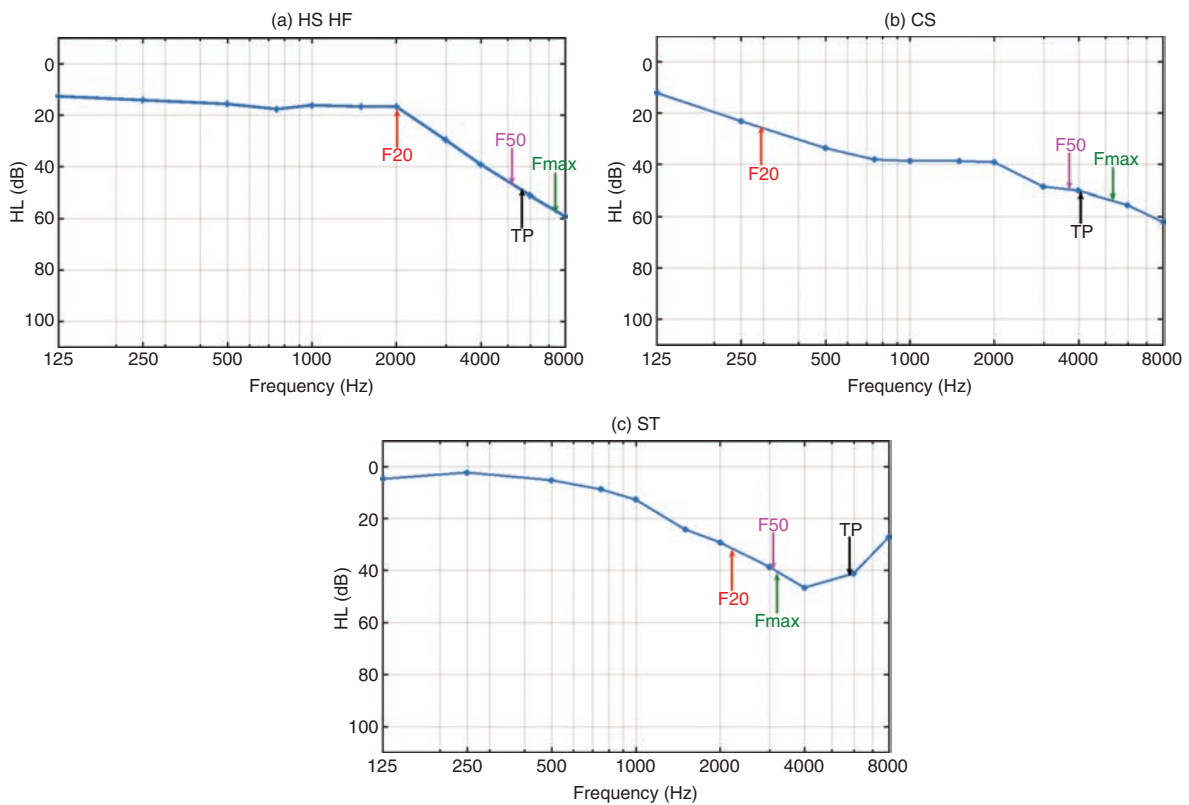


Figure 10: Scatter plot of (a) F20 versus TP, (b) F50 versus TP, and (c) Fmax versus TP, for high-steep high-frequency HL subtype.

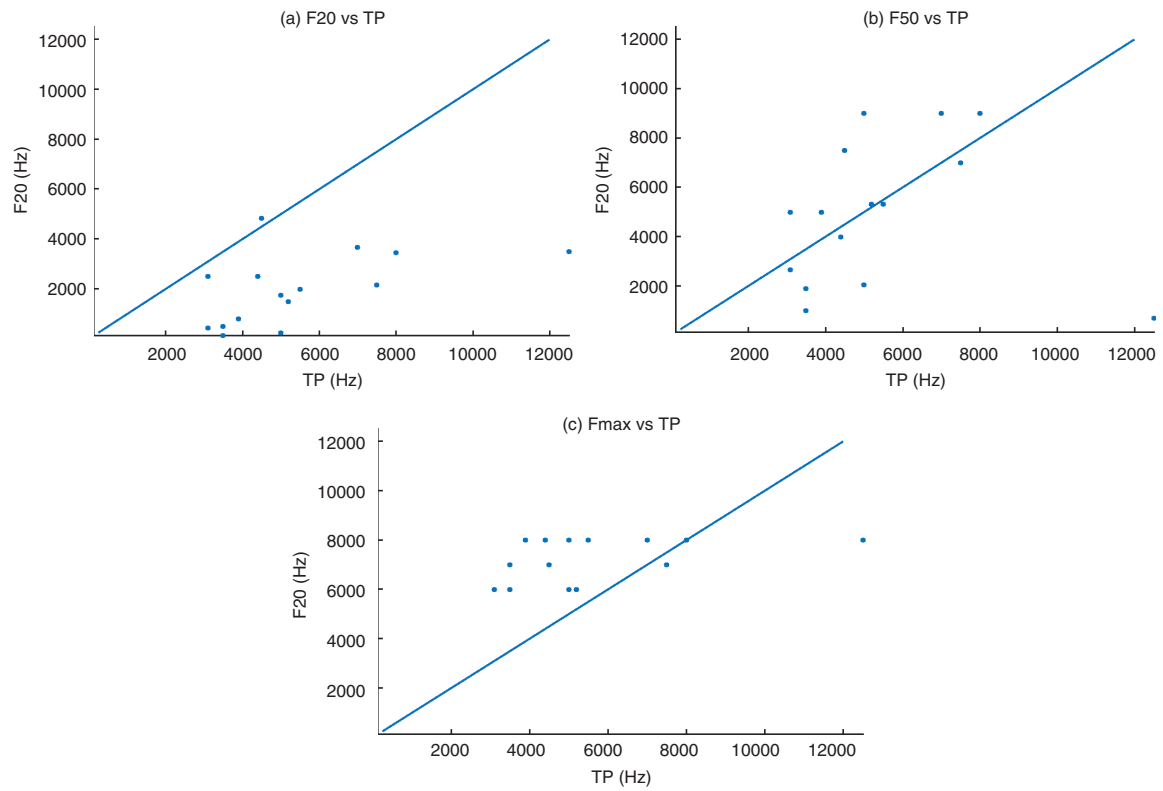


Figure 11: Scatter plot of (a) F20 versus TP, (b) F50 versus TP, and (c) Fmax versus TP, for continuously steep HL subtype.

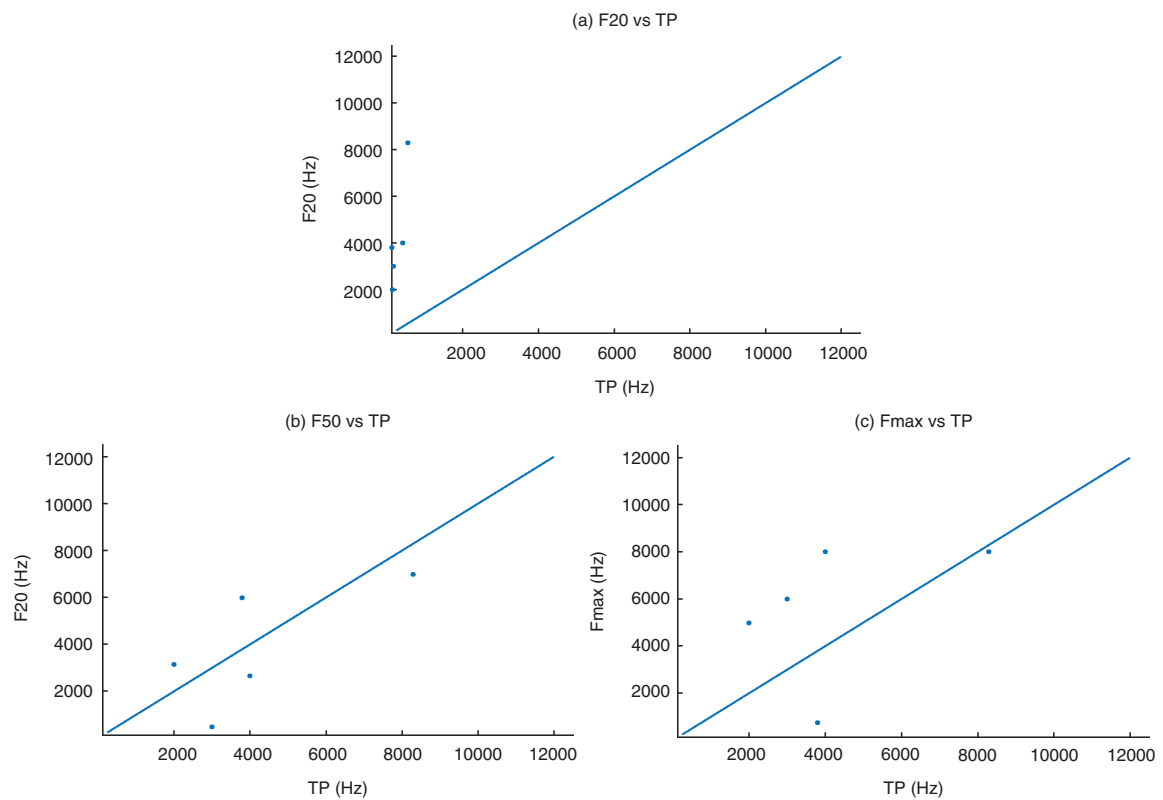


Figure 12: Scatter plot of (a) F20 versus TP, (b) F50 versus TP, and (c) Fmax versus TP, for HL with scotoma subtype.

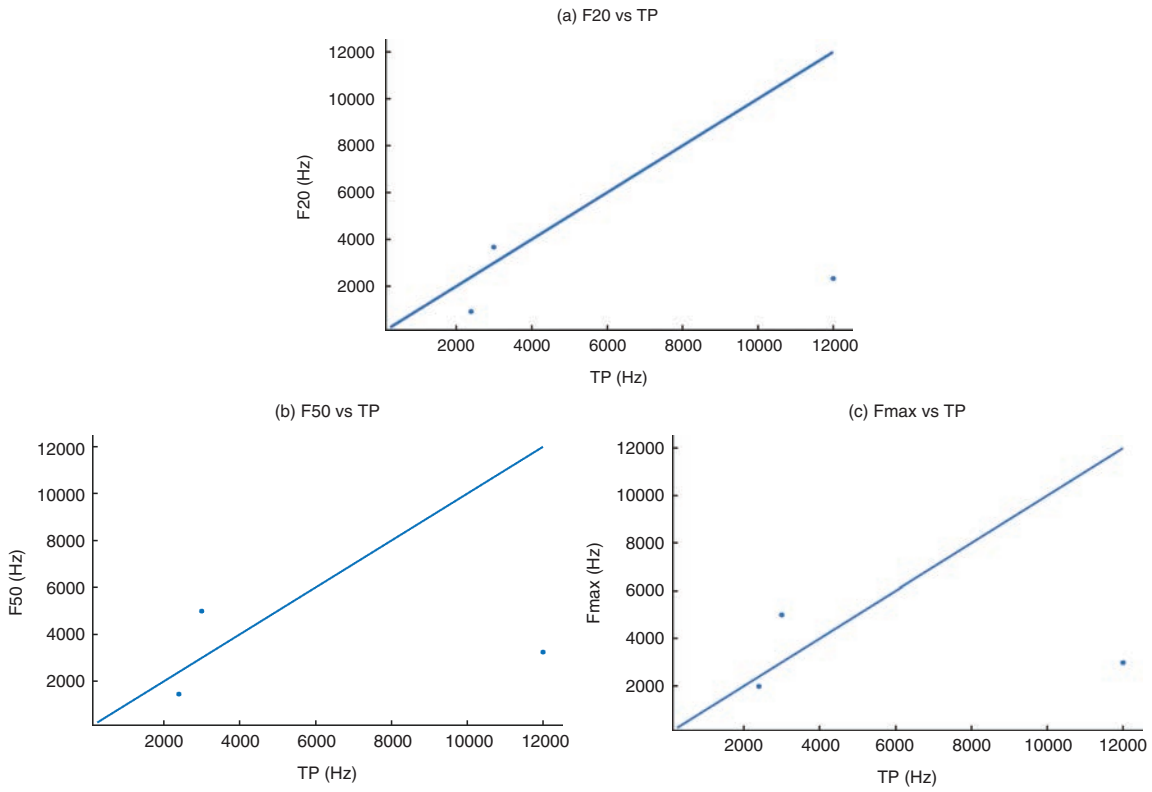


Figure 13: Scatter plot of (a) F20 versus TP, (b) F50 versus TP, and (c) Fmax versus TP, for high steep high-frequency (blue) and continuously steep (red) HL subtypes.

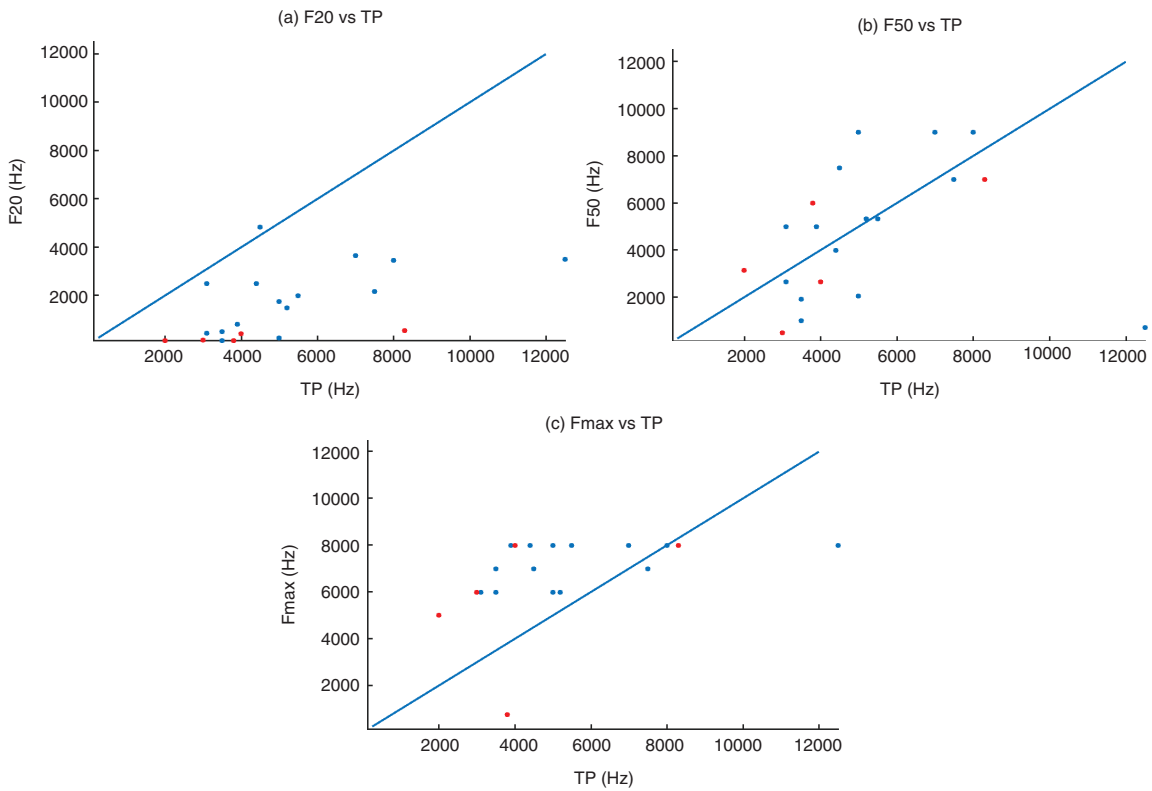


Table 4: Spearman rank correlation analysis between paired audiometric-tinnitus variables for the subjects with HS and CS HL subtypes.

<i>Paired variables</i>	<i>r</i>	<i>p</i>
F20 versus TP	0.59	0.006
F50 versus TP	0.49	0.027
Fmax versus TP	0.65	0.002

and CS HL subgroup. As it can be seen, there exists a positive correlation between audiometric (moderate for F20 and F50 and strong for Fmax) and tinnitus (TP) features.

4. DISCUSSION

Our categorization of HL subtypes (Figure 6) is slightly different to that of Nicolas-Puel et al. (2002). In a similar way to them, we consider high-steep high-frequency and flat HL subtypes. However, the other two subtypes, namely, continuously steep and scotoma HL, could differ of the low-frequency HL and dead ear considered by Nicolas-Puel et al. König et al. (2006) and Shekhawat et al. (2014) only considered tinnitus subjects with high-steep high-frequency HL and continuously steep HL, respectively. Serena et al. (2011), on the other hand, distinguished between 0-break “broken-stick” HL (similar to our flat HL), 1-break “broken-stick” (similar to our HS HL), and 2-break “broken-stick”, without matching to our subgroups. Langguth et al. (2017) defined four HL subgroups; namely (1) normal hearing (0–20 dB HL); (2) mild/moderate HL (25–50 dB HL), representing mostly outer hair cell loss; (3) severe/profound HL (>50 dB HL), representing outer and inner hair cell damage; and (4) no data available.

The most prevalent HL subtype in our cohort is high-steep high-frequency HL (44%), followed by flat HL (32%), continuously steep HL (15%) and scotoma HL (9%). If HS and CS would be included in a joint subtype, then the prevalence of both should be 59%. Regarding the flat HL curves, it might be emphasized that we have measured just up to 8 kHz. Therefore, HL flat up to 8 kHz does not exclude the occurrence of losses above 8 kHz which can potentially trigger tinnitus, mainly at high frequencies (Weisz et al., 2006). High frequency losses (8–16 kHz) have been recently interpreted as an early indication of cochlear synaptopathy in humans (Milloy et al., 2017). Cochlear synaptopathy, also named hidden HL, is the selective loss of synaptic connections between high-threshold and low-spontaneous rate IHCs with the auditory nerve, showing or not threshold elevations, due to the loss of hair cells-auditory nerve synaptic connection (Lieberman & Liberman, 2015). The loss of these connections can reach 40–50% without elevating hearing thresholds. As HL is considered the most likely trigger of tinnitus, this subgroup is further excluded of the correlational analysis between audiometric and tinnitus features.

Concerning the tinnitus lateralization (Figure 7a), surprisingly 43% of subjects with HS, CS, or ST HL

perceived their tinnitus in the left ear, in contrast to subjects perceiving their tinnitus in the right ear, only 8%. In the cohort of Scheklmann et al. (2012) there was also a bias toward the left ear (72 versus 45 subjects). In the cohort of Shekhawat et al. (2014), on the contrary, 103 participants had the predominant tinnitus towards the right ear, versus 83 subjects with their tinnitus towards the left ear. Therefore, the high bias of the unilateral tinnitus towards the left ear in our cohort might be considered merely casual.

The tinnitus sound of our sample differs also from other databases. In our cohort (Figure 7b), pure tone and ringing have a similar prevalence (39% and 35%, respectively), while hissing is less prevalent (26%). In the Tinnitus Archive of the Oregon Health State University (OHSU), tonal, ringing, and hissing are also the more frequent tinnitus sounds, but with a different prevalence. When more than one predominant sound is reported, ringing is prominently the more prevalent sound.

Notice also that, when flat HL subtype is excluded, sensorineural HL is the most possible origin of tinnitus referred by participants (39%), followed by noise (30%) (Figure 7c).

Our results concur with those of Shekhawat et al. (2014) regarding the audiometric feature which correlates better with the tinnitus pitch (Figures 8 and 9), at least for the HS and CS HL subtypes. In effect, our results confirm that F20 (the frequency at which audiometry crosses HL=20 dB) and Fmax (the frequency at which HL is maximum) under- and overestimate, respectively, the tinnitus pitch. Spearman rank correlation analysis confirms that tinnitus pitch increases monotonically with F20, F50, and Fmax (Figures 10–12 and Table 4), but that it is better correlated with F50. This corroborates the hypothesis that tinnitus pitch is matched to the frequency at which hearing loss reaches 50 dB HL (Shekhawat et al., 2014).

5. CONCLUSIONS

This article contains a preliminary correlational study between audiometric characteristics and tinnitus features in a sample of 34 human subjects with tinnitus. Following the current trend of tinnitus heterogeneity, subjects are categorized first in four subgroups, taking into account the shape of HL curves, namely flat HL, high-steep high-frequency HL, continuously steep HL, and HL with scotoma. The more prevalent subgroup was the high-steep high-frequency HL. Excluding the flat HL subgroup, three audiometric features are calculated from the HL curves: F20, the frequency at which HL=20 dB, F50, the frequency at which HL=50 dB, and Fmax, the frequency at which HL is maximum.

Tinnitus characteristics include tinnitus laterality (left ear, right ear, bilateral, or central), tinnitus sound (tonal, ringing, or hissing), tinnitus etiology, THI, VAS, and tinnitus pitch (TP). Tinnitus laterality, sound, and etiology were evaluated by the responses of participants to an interview. TP was assessed by matching the tinnitus of participants to a band-filtered noise generated by a GUI.

Depending on the bandwidth of the filter, tones (very narrow), ringing (narrow), or hissing (wide) sounds were generated.

Correlational studies included paired audiometric-tinnitus variables analysis. Spearman rank correlation analysis confirmed that TP increases monotonically with the three audiometric variables. Mean variables, TP-F20, TP-F50, and TP-Fmax were also analyzed. Results demonstrated that F20 underestimates TP, Fmax overestimates TP, and F50 is the best estimator of TP. Therefore, our results confirm that F50, the frequency at which IHC damage begins, is likely the best predictor of the associated tinnitus pitch.

ACKNOWLEDGMENTS

The enthusiastic participation of volunteers in this study is kindly recognized. Financial support was provided by CSIC through grant 201750E037.

REFERENCES

- Cobo, P. (2015). Tinnitus: Mechanisms, measures and sound treatments. *Loquens*, 2, e024. <https://doi.org/10.3989/loquens.2015.024>
- Diges, I., Simón, F., & Cobo, P. (2017). Assessing auditory processing deficits in tinnitus and hearing impaired patients with the Auditory Behavior Questionnaire. *Frontiers in Neuroscience*, 11, 187. <https://doi.org/10.3389/fnins.2017.00187>
- Eggermont, J. J. (2012). *The neuroscience of tinnitus*. Oxford: Oxford University Press. <https://doi.org/10.1093/acprof:oso/9780199605606.001.0001>
- Eggermont, J. J. (2014). *Noise and the brain*. Amsterdam: Elsevier. <https://doi.org/10.1016/B978-0-12-415994-5.00011-7>
- Eggermont, J. J., & Tass, P. A. (2015). Maladaptive neural synchrony in tinnitus: Origin and restoration. *Frontiers in Neurology*, 6, 29. <https://doi.org/10.3389/fneur.2015.00029>
- Hall, D. A., Haider, H., Kikidis, D., Mielczarek, M., Mazurek, B., Szczepek, A. J., & Cederroth, C. R. (2015). Toward a global consensus on outcome measures for clinical trials in tinnitus. *Trends in Amplification*, 19, 1–7. <https://doi.org/10.1177/2331216515580272>
- Herráiz, C., Hernández Calvin, F. J., Plaza, G., Tapia, M. C., & de los Santos, G. (2001). Evaluación de la incapacidad en los pacientes con acúfenos. *Acta Otorrinolaringológica Española*, 52, 142–145. [https://doi.org/10.1016/S0001-6519\(01\)78247-7](https://doi.org/10.1016/S0001-6519(01)78247-7)
- Kleinjung, T., Steffens, T., Struz, J., & Langguth, B. (2009). Curing tinnitus with a Cochlear Implant in a patient with unilateral sudden deafness: A case report. *Cases Journal*, 2, 7462. <https://doi.org/10.1186/1757-1626-2-7462>
- König, O., Schaette, R., Kempster, R., & Gross, M. (2006). Course of hearing loss and occurrence of tinnitus. *Hearing Research*, 221, 59–64. <https://doi.org/10.1016/j.heares.2006.07.007>
- Langguth, B., Landgrebe, M., Schlee, W., Schecklmann, M., Vielsmeier, V., Steffens, T., Staudinger, S., Frick, H., & Frick, U. (2017). Different Patterns of hearing loss among Tinnitus Patients: a latent class analysis of a large sample. *Frontiers in Neuroscience*, 8, 46. <https://doi.org/10.3389/fneur.2017.00046>
- Liberman, L. D., & Liberman, C. M. (2015). Dynamics of cochlear synaptopathy after acoustic overexposure. *Journal of the Association Research of Otolaryngology*, 16, 205–219. <https://doi.org/10.1007/s10162-015-0510-3>
- Milloy, V., Fournier, P., Benoit, D., Noreña, A., & Koravand, A. (2017). Auditory brainstem responses in tinnitus: A review of who, how, and what? *Frontiers in Aging Neuroscience*, 9, 237. <https://doi.org/10.3389/fnagi.2017.00237>
- Nicolas-Puel, C., Lloyd Faulconbridge, R., Guitton, M., Puel, J. L., Mondain, M., & Uziel, A. (2002). Characteristics of tinnitus and etiology of associated hearing loss: A study of 123 patients. *International Tinnitus Journal*, 8, 37–44.
- Noreña, A. J. (2011). An integrative model of tinnitus based on a central gain controlling neural sensitivity. *Neuroscience and Biobehavioral Reviews*, 35, 1089–1109. <https://doi.org/10.1016/j.neubiorev.2010.11.003>
- Roberts, L. E., Bosnyak, D. J., Bruce, I. C., Gander, P. E., & Paul, B. T. (2015). Evidence for differential modulation of primary and nonprimary auditory cortex by forward masking in tinnitus. *Hearing Research*, 327, 9–27. <https://doi.org/10.1016/j.heares.2015.04.011>
- Roberts, L. E., Moffat, G., & Bosnyak, D. J. (2006). Residual inhibition functions in relation to tinnitus spectra and auditory threshold shift. *Acta Otolaryngol. (Stockh)*, 126, 27–33. <https://doi.org/10.1080/03655230600895358>
- Schecklmann, M., Vielsmeier, V., Steffens, T., Landgrebe, M., Langguth, B., & Kleinjung, T. (2012). Relationship between audiometric slope and tinnitus pitch in tinnitus patients: Insights into the mechanisms of tinnitus generation. *PLOS One*, 7, e34878. <https://doi.org/10.1371/journal.pone.0034878>
- Sereda, M., Hall, D. H., Bosnyak, D. J., Edmondson-Jones, M., Roberts, L. E., Adjamian, P., & Palmer, A. R. (2011). Re-examining the relationship between audiometric profile and tinnitus pitch. *International Journal of Audiology*, 50, 303–312. <https://doi.org/10.3109/14992027.2010.551221>
- Shekhawat, G. S., Searchfield, G. D., & Stinear, C. M. (2014). The relationship between tinnitus pitch and hearing sensitivity. *Eur. Arch. Otolaryngol.*, 271, 41–48. <https://doi.org/10.1007/s00405-013-2375-6>
- Van de Heyning, P., Meeus, O., Blaivie, C., Vermeire, K., Boudewyns, A., & De Ridder, D. (2007). Tinnitus: a multidisciplinary clinical approach. *B-ENT* 3, 3–10.
- Vio, M. M., & Holme, R. H. (2005). Hearing loss and tinnitus: 250 million people and US\$10 billion potential market. *Drugs Discovery Today*, 10, 1263–1265. [https://doi.org/10.1016/S1359-6446\(05\)03594-4](https://doi.org/10.1016/S1359-6446(05)03594-4)
- Weisz, N., Hartmann, T., Dohrmann, K., Schlee, W., & Noreña, A. (2006). High-frequency tinnitus without hearing loss does not mean absence of deafferentation. *Hearing Research*, 222, 108–114. <https://doi.org/10.1016/j.heares.2006.09.003>