



# Asymmetry of Occupational Noise Induced Hearing Loss: An Electrophysiological Approach

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Int Arch Otorhinolaryngol 2023;27(3):e499–e510.

## Abstract

**Introduction** The question as to whether occupational noise exposure causes symmetrical or asymmetrical hearing loss is still controversial and incompletely understood.

**Objective** Two electrophysiological methods (cortical evoked response audiometry: CERA and auditory steady state responses: ASSR) were used to address this issue.

**Method** 156 subjects with a well-documented history of noise exposure, a wide range of noise induced hearing loss (NIHL) and without middle ear pathology underwent both a CERA and an ASSR examination in the context of an exhaustive medicolegal expert assessment intended for possible compensation.

**Results** Whatever the method (CERA or ASSR), the average electrophysiological hearing thresholds (1-2-3 kHz) are significantly worse in the left ear. The right - left differences in CERA and ASSR thresholds are strongly correlated with each other. No significant effect of frequency is found. No correlation is observed between right - left differences in hearing thresholds and either age or degree of hearing loss.

**Conclusion** In NIHL, there is an actual average right - left difference of about 2.23 dB, i.e., 3.2%, the left ear being more impaired.

## Keywords

- ▶ hearing loss
- ▶ asymmetry
- ▶ evoked potentials
- ▶ noise

## Introduction

Occupational noise-induced hearing loss (NIHL) has traditionally been defined as a symmetrical, sensorineural hearing loss, with the earliest and most important loss being between 3 and 6 kHz.<sup>1</sup>

However, there is some controversy on the question of symmetry. There may be unequal noise exposure between the left and right ears, for example, in the case of shoulder weapon noise exposure (head shadow effect).<sup>2-4</sup>

Such lateralized occupational activities are, nevertheless, rather uncommon. Several authors investigating occupational NIHL failed to find evidence for the statement that one ear is more vulnerable to NIHL than the other.<sup>5-7</sup>

Masterson et al.<sup>8</sup> performed a systematic review of the literature on NIHL in people demanding compensation, focusing on asymmetrical hearing thresholds. Their criterion for asymmetry was > 15 dB for any frequency between 0.5 and 8 kHz. In a pooled sample of 4,735 individual cases, asymmetrical hearing loss accounted for between 2.4 and 22.6% of NIHL cases.

However, also aiming to determine whether occupational noise exposure causes symmetrical or asymmetrical hearing loss, Sturman et al.<sup>1</sup> investigated 83 subjects with occupational NIHL (claimants for compensation) and observed a hearing threshold at 3 kHz, significantly higher in the left ear than in the right ear, statistically (2.41 dB).

received

October 1, 2021

accepted after revision

May 15, 2022

article published online

March 29, 2022

DOI <https://doi.org/>

10.1055/s-0042-1750766.

ISSN 1809-9777.

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With the idea to control for asymmetric exposure, Pirilä<sup>9</sup> observed that the temporary threshold shifts in young adults were higher in the left than in the right ears after exposition to symmetrical broad band noise for a maximum of 8 hours.

Thus, the question of NIHL asymmetry remains open for discussion.

However, all of the above data relied on traditional pure tone audiometry (PTA), and possibly performed in a context of occupational (i.e., non-clinical) medicine. Few studies have used an electrophysiological approach of a possible asymmetry in NIHL.

Aboobackr et al.<sup>10</sup> compared brainstem evoked response audiometry (BERA) results in 31 stone cutting workers (mean age 28) with exposure to noise > 85 dB at their workplace, with those of 30 controls without exposure to noise. Modal BERA-threshold values were 60 dB and 40 dB for cases and controls respectively. When comparing the noise exposed subjects to the controls, BERA's absolute peak latencies (I, III, and V) measured at 90 dB showed significantly higher mean values for the left-hand side in the exposed subjects. For the right-hand side, only the absolute latency of peak I was significantly higher in the exposed subjects. However, none of the interpeak latencies were significantly different when compared between exposed and non-exposed subjects. The authors concluded that there are higher BERA abnormalities in the left ear, but that in NIHL it is the peripheral/cochlear component of auditory pathway that were affected while the neural and retroneural stations remained normal. This is in line with previous observations of Attias et al.<sup>11</sup> regarding machine operators: there were modifications in the absolute latencies of the early waves, without significant influence on central neural conduction. Recently, Xiao et al.<sup>12</sup> reported higher weighted values of PTA and auditory steady-state response (ASSR) in left ears when compared to the right ears of Chinese workers (41.8 +/- 7.6 years; 10.1 +/- 6.2 years noise exposure).

In a previous prospective study,<sup>13</sup> we compared two electrophysiological techniques, ASSRs and cortical evoked response audiometry (CERA), to objectively estimate frequency-specific thresholds in adults undergoing an expertise examination for medicolegal and/or compensation purposes in case of NIHL. Both techniques were used in the same 156 subjects with well documented exposure to noise. Relevant thresholds for compensation in this context are 1, 2, and 3 kHz.

The study was set up to clarify the correlation between the thresholds obtained by the two electrophysiological methods. In the present study, this unique dataset is exploited to bring a genuine contribution to the intriguing issue of the right and left asymmetry of NIHL. The ASSRs and CERA tests rely upon different processing techniques of the electrical activity of the auditory pathways in reaction to sound stimuli.

The CERA (also called slow vertex responses) has been used for more than 30 years in our institution for objective definition of auditory thresholds.<sup>13-18</sup> Stimuli consist of 50 milliseconds tone bursts repeated at a rate of 1 Hz (50 to 250 sweeps for one tracing). Four separate tracings are super-

imposed for each tested intensity at a given frequency. A typical response pattern is observed: P1 (50–80 milliseconds); P2 (150–200 milliseconds); N2 (180–300 milliseconds). Near the threshold, latencies increase and the signal-to noise ratio decreases. However, CERA overestimates the actual (psychophysiological) hearing thresholds: the difference scores for CERA-PTA in (supposedly) fully reliable subjects with NIHL, are approximately 13, 10, and 9 dB<sub>HL</sub> for the frequencies of 1, 2, and 3 kHz respectively.<sup>14,19</sup>

The ASSRs are electrophysiological responses to auditory stimuli presented at rates between 1 and 200 Hz or by periodic modulations (at similar rates) of the amplitude and/or frequency of a continuous (steady state) tone. This tone is characterized by a specific frequency, the so-called carrying frequency (CF). It is possible to record auditory steady state responses from electrodes on the scalp. The EEG signal is amplified approximately 80,000 times and a band-pass of 5 to 100 Hz is applied for filtering. The ASSR is occurring at the same rate as the modulation frequency, hence it is suited for analysis by frequency-domain methods. The spectrogram of the response reveals a peak at the modulation frequency.<sup>20</sup> The ASSRs can be objectively detected using frequency-based analyses.<sup>21-23</sup> The presence of an ASSR depends on the properly functioning of both auditory peripheral structures (cochlea and auditory nerve) for the CF, and central auditory pathways.<sup>20</sup>

In conscious subjects, the ASSRs are particularly identifiable at modulation rates around 40 Hz.<sup>21</sup> At these rates, the response is supposed to be primarily generated at the cortical level,<sup>22,23</sup> with contributions of brainstem, auditory midbrain, and thalamus.<sup>24-28</sup>

D'Haenens et al.<sup>29</sup> showed that ASSR thresholds demonstrate excellent test and retest reliability for all frequencies (0.5, 1, 2, and 4 kHz).

However, similarly to CERA, ASSRs overestimate the behavioral thresholds.<sup>30-32</sup> Also, a systematic shift has been noticed, with ASSR thresholds being on average 4.38 dB better (i.e., showing less hearing loss) than CERA-thresholds.<sup>13</sup>

## Material and Methods

### Design and Protocol

In the present study, 156 successive claimants for compensation at the Federal Agency for Occupational Risks (FEDRIS, Brussels) and fitting our inclusion criteria were included, running over 50 months. In all cases, the occupational career was checked by the Engineering Department of FEDRIS prior to medical examination, to reasonably accept a noise exposure of at least two years to at least 85 dB<sub>A</sub> Leq (Leq refers to the sound level in dB<sub>A</sub> having the same total sound energy as the fluctuating level measured). Main occupational activities were: construction (buildings, roads etc.), 52; metallurgy, 42; welding, 14; automobile industry, 11; lorry driving, 10; forestry / garden maintenance, 7; industrial cleaning, 6; glass factory, 4; shipbuilding, 3; firefighting, 2; weapon factory, 2; aircraft factory, 2; music, 1. Furthermore, in each individual case, a very detailed inventory of successive occupations was

set up, which revealed that in nearly all cases, the subject had been exposed, throughout his career, to various types of occupational noise, and usually in different ways (mean duration of exposure: 27 years).

As a rule, every claim for NIHL compensation at FEDRIS must be supported by an (external) audiological assessment. The claimant then receives an appointment for a medicolegal expertise including a new audiometry at FEDRIS. In case of a significant discrepancy between the results of the two PTAs, suggesting exaggeration—which was the main inclusion criterion of our previous study—the claimant was given a new appointment, usually a few weeks later, for another PTA, followed by an objective electrophysiological assessment. This electrophysiological assessment consisted in both a CERA and an ASSR definition of hearing thresholds, with frequency specificity. The examination was completed both the first and the second time by a tympanometry—a recording of the acoustic stapedial reflexes. When relevant and possible, they were also submitted to a Békésy audiometry and a prosthetic audiometry. However, due to their lack of reliability (which was the motivation for carrying out the CERA/ASSR), the behavioral PTA thresholds were not taken into account in the present study. In a previous study, we showed that they may be estimated on average 13, 12.7, and 10.4 dB lower (better) than the ASSR thresholds for 1, 2, and 3 kHz, respectively.<sup>32</sup>

All subjects received adequate information about the different examination procedures. No subject refused the examinations. It should be recalled that they are claiming for compensation, and that they are asking, themselves, for a medical-forensic expert examination. In a medicolegal context, any invasive procedure is clearly ruled out. All data were strictly anonymized, according to the standard rules and procedures applicable for scientific studies within FEDRIS.

Prior to any investigation, each subject underwent a bilateral otoscopy to rule out ear wax or any foreign object. Further exclusion criteria were middle ear pathology and conductive hearing loss (either uni- or bilateral), poor health, cognitive impairment, or difficulties in communicating due to language problems. Age, gender, and duration of exposure were systematically recorded. The overwhelming majority of the subjects were male (147/156).

In the case of no measurable threshold, whatever the method (i.e., no response at maximal level of stimulus), the threshold was considered to be 120 dB<sub>HL</sub>. For ASSR, only octave frequencies are available, that is, 0.250, 0.500, 1, 2, and 4 kHz (pure tone). For 3 kHz, the arithmetical mean between the thresholds at 2 and 4 kHz was considered for computations. It has been shown that, for epidemiological studies involving large amounts of data, the interpolated threshold may be considered as a valid estimate of the true value of the 3 kHz threshold.<sup>33</sup>

For CERA, a Bio-Logic Navigator PRO system (Bio-logic Systems Corp. Orlando, FL, USA) was used, with the following parameters: stimulus 50 milliseconds tone-burst, 1 / s; filtering 0,1 to 10 Hz; analysis epoch: 600 milliseconds; #

stimuli: 50 to 250. Then, CERA responses were recorded four times at each intensity level. As in our previous work,<sup>13–16</sup> the criterion for defining a CERA threshold was the lowest stimulus intensity (in dB HL, steps of 5 dB) evoking an unequivocal averaged response, that is to say, the expected pattern P1-P2-N2 clearly identified when superimposing four displayed averaged CERA tracings obtained with identical stimulations: amplitude 2 to 10  $\mu$ V; P1 (50–80 milliseconds); P2 (150–200 milliseconds); and N2 (180–300 milliseconds).

The ASSRs data were obtained using a Neuro-Audio.Net system (Neurosoft Ltd., Ivanovo, Russia). Stimuli were pure tones (0,5–4 kHz), 100% amplitude, and 10% frequency modulation, with modulation frequency being around 46 Hz. In ASSR, an adaptive recording algorithm prevents such an interpretation: after the stimulation has started, the algorithm seeks for a significant response in each of the channels. As soon as the level of significance is reached, the algorithm stops the recording in this particular channel (e.g., 55 dB at 2 kHz left), whereas recording continues in the other channels. In the channel wherein a significance is reached, the stimulation automatically restarts with a 5 dB lower intensity, and the process is repeated until no significant response is obtained after 6 minutes. The time progress of the eight channels is permanently displayed, and the system also displays an audiogram. This process avoids any subjective interpretation.

For electrophysiological testing, the subject was lying on an examination couch, in a relaxed position, with the head resting on a pillow, and remained awake for the duration of the test. Impedance checks were completed for all electrodes (< 5 k $\Omega$ ). The audiologist was sitting beside the subject, within the soundproof booth, operating the computer and continually controlling the subject's alertness.

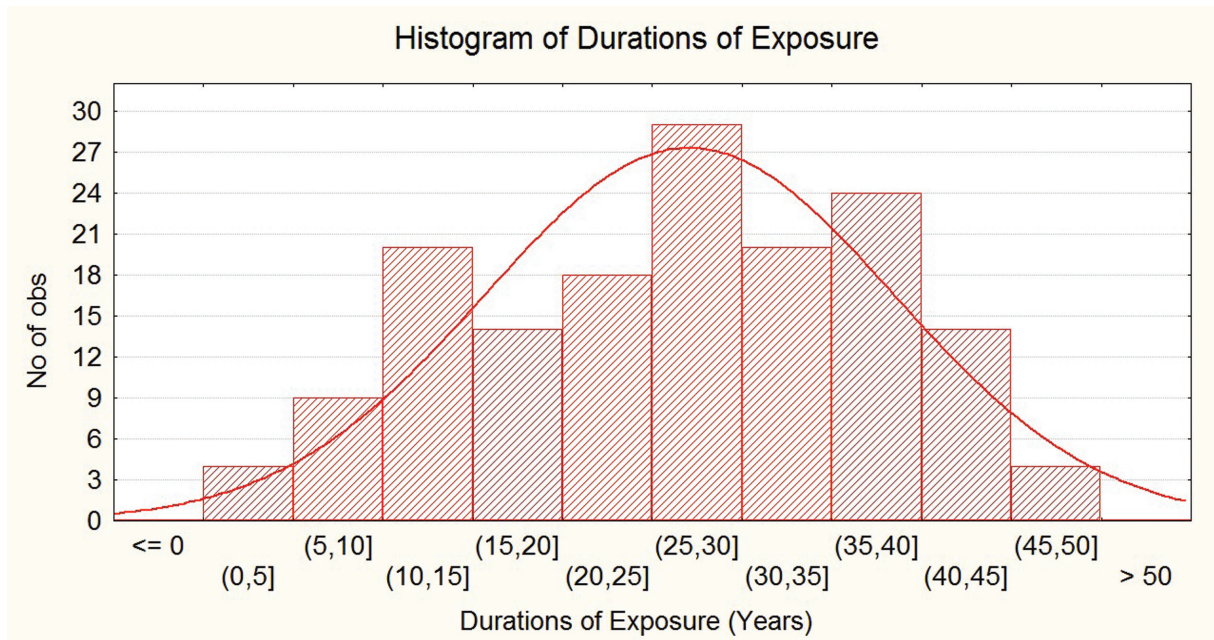
Conventional as well as electrophysiological audiometric procedures were performed in a soundproof booth (background noise measured inside 27 dB<sub>A</sub>), also operating as a Faraday cage. Acoustic stimuli were provided to the subject via two TDH-39 headphones (Telephonics, Farmingdale, NY, United States).

In a few cases, provoked otoacoustic emissions could be recorded, but this succeeded only in a very small proportion of our subjects, which is not surprising when considering the average level of hearing losses (see below). These data have not been taken into account.

The present study is retrospective. All subject data were strictly anonymized, according to the standard rules and procedures applicable for scientific studies within FEDRIS. Our institute has no ethics committee, but a General Data Protection Regulation (GDPR) board who has formally approved the study.

## Results

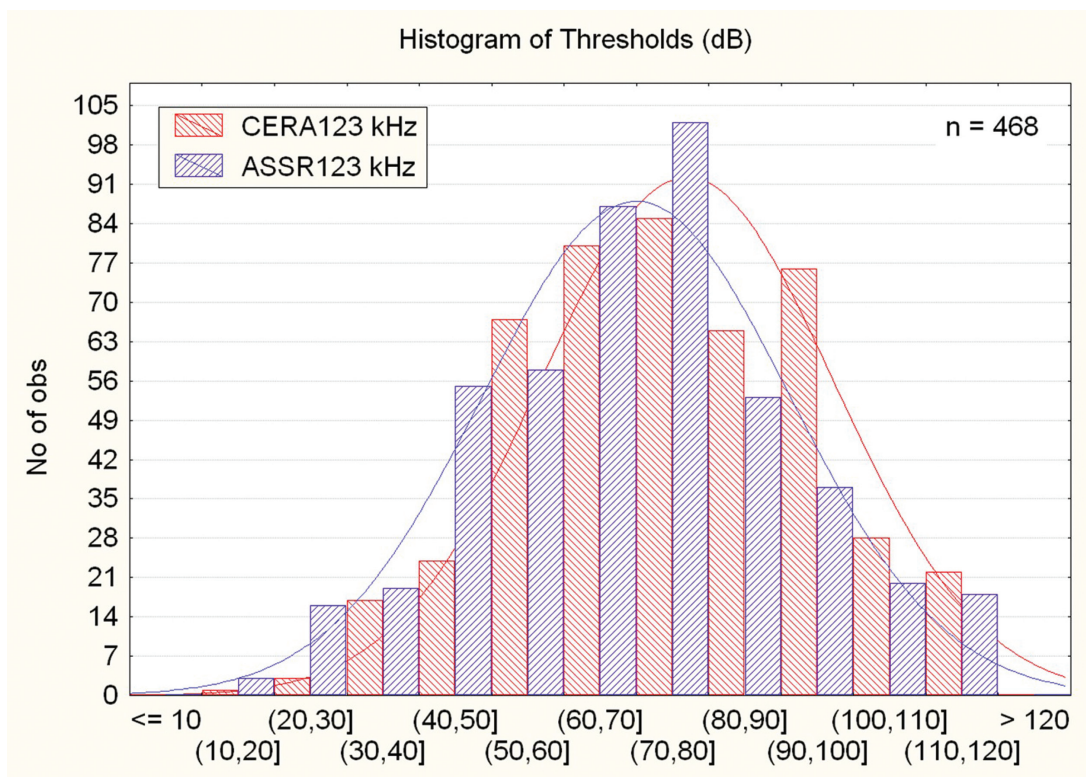
The age distribution of our 156 subjects is typically gaussian, with most of the subjects in the age groups from 55 to 70 years. Mean age is 63.4 years  $\pm$  10.0 (SD).



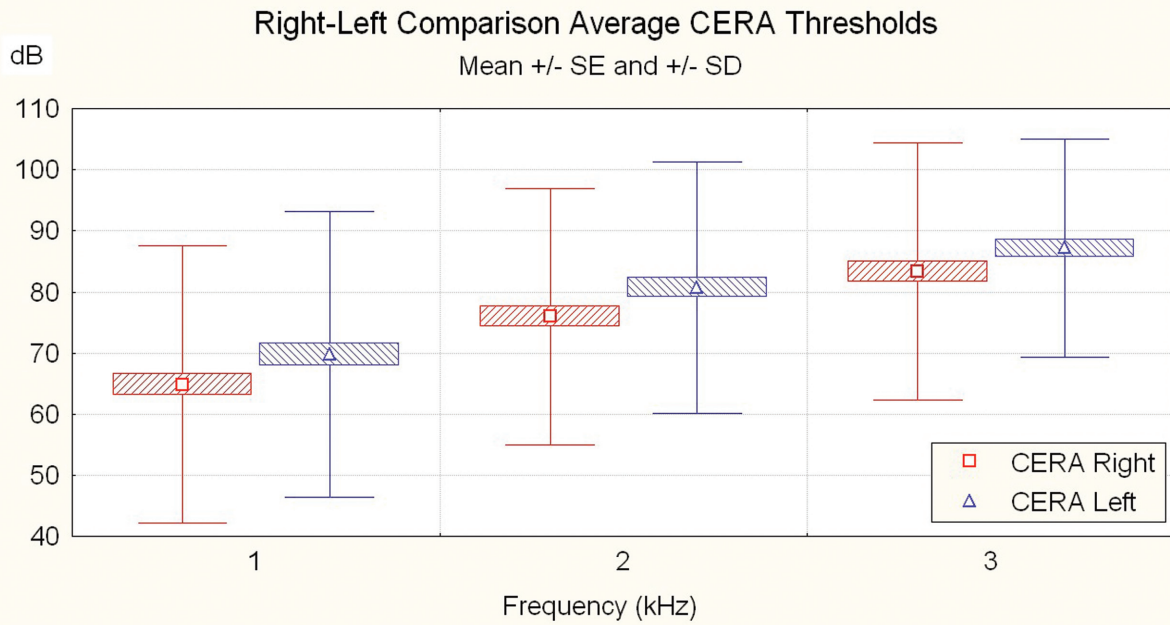
**Fig. 1** Histogram of durations of exposure to noise; The mean is 27 years  $\pm$  11.4 (SD).

The main duration of exposure to noise ranges was between 25 and 40 years, although with a broad dispersion, as can be seen in the histogram of **Fig. 1**. The mean is 27 years  $\pm$  11.4 (SD).

**Fig. 2** shows a histogram of hearing thresholds (dB) at 1, 2, and 3 kHz, as measured by CERA and ASSR, respectively. In each subject, the thresholds for the right and the left ear have been averaged. For each technique, 468 threshold values are



**Fig. 2** Histogram of hearing thresholds (dB) at 1, 2, and 3 kHz, measured by CERA and ASSR respectively. In each subject, the thresholds for the right and the left ear are averaged. For each technique, 468 threshold values are considered. Distributions are gaussian. On average, CERA thresholds are slightly higher than ASSR thresholds.



**Fig. 3** Average CERA thresholds (+/- 1 standard error and 1 standard deviation) at 1, 2, and 3 kHz, for the right and left ear respectively (n = 156). The average hearing loss increases with frequency, as expected in NIHL (p < 0.001). The left threshold is on average always higher than the right one (see ►Table 1).

**Table 1** Average right and left threshold values (+/- 1 SD), per frequency, for CERA and ASSR

	Right (dB) +/- 1 SD	Left (dB) +/- 1SD
CERA 1 kHz	64.87 +/- 22.65	69.81 +/- 23.39
CERA 2 kHz	75.99 +/- 20.99	80.77 +/- 20.57
CERA 3 kHz	83.37 +/- 21.08	87.18 +/- 17.92
ASSR 1 kHz	61.31 +/- 24.60	63.62 +/- 24.19
ASSR 2 kHz	69.87 +/- 24.47	71.89 +/- 21.47
ASSR 3 kHz	75.35 +/- 21.44	77.71 +/- 18.73
ASSR 4 kHz	80.83 +/- 21.33	83.53 +/- 18.20

considered. Distributions are gaussian. On average, CERA thresholds are slightly higher than ASSR thresholds (77 +/- 20.24 dB versus 69,95 +/- 21.22 dB).

►Fig. 3 compares the average CERA thresholds (+/- 1 standard error and 1 standard deviation) at 1, 2, and 3 kHz, for the right and the left ears respectively (n = 156). The average hearing loss increases with frequency, as expected in NIHL (Spearman ρ = 0.33 for the right side and 0.33 for the left side; both p < 0.0001). Comparative values and SDs are given in ►Table 1.

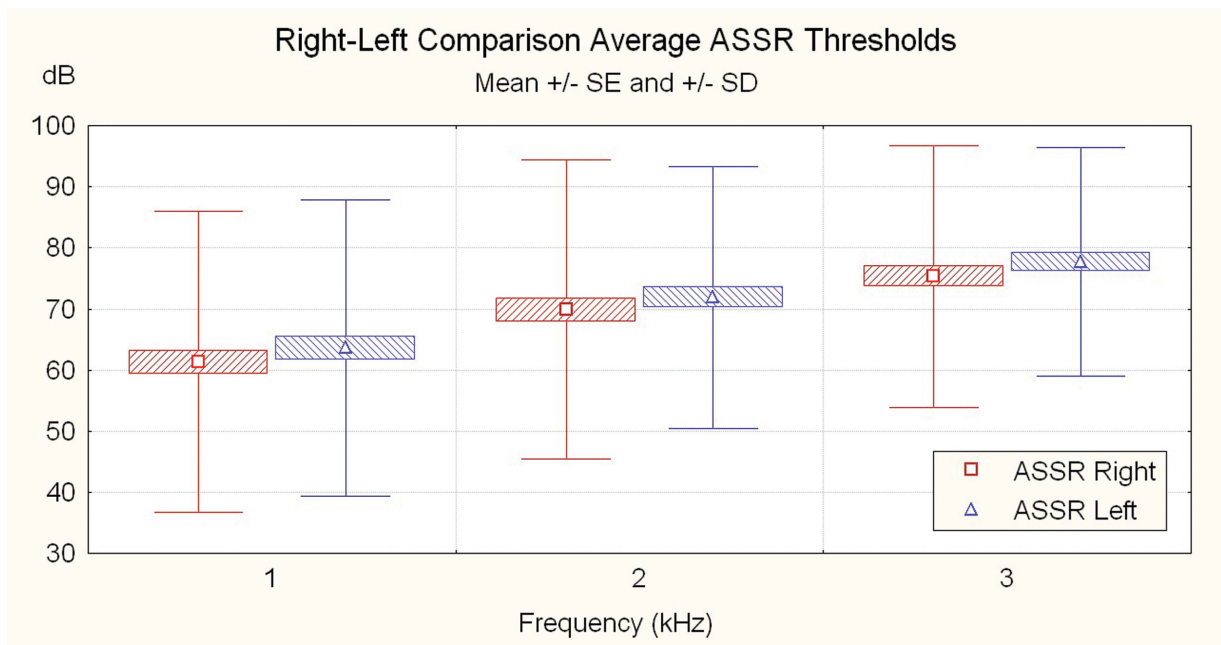
►Fig. 4 is similar to ►Fig. 3 for the average ASSR thresholds. Again, the average hearing loss increases with frequency, as expected in NIHL (Spearman’s ρ = 0.23 for the right-hand side and 0.28 for the left-hand side; both p < 0.0001). Comparative values and SDs are given in ►Table 1.

The global correlation between the CERA and ASSR thresholds (3 thresholds per ear) is plotted in ►Fig. 5. The r value (0.72) is highly significant (p < 0.0001; n = 468).

►Fig. 6 gives an overview of the mean threshold values (+/- 1 and 1,96 standard error) at 1, 2, and 3 kHz for ASSR and CERA and in right and left ears respectively. For ASSR, 4 kHz is also available.

When the threshold values for the three critical frequencies are grouped, the right and left differences (T-test for dependent variables) become clearly significant, although they are stronger for CERA than for ASSR: p = 0.000001 for CERA and p = 0.011 for ASSR. If, for ASSR the frequencies 1, 2, and 4 kHz are grouped, the p-value becomes 0.009. Grouped, mean CERA-values (1–2–3 kHz) are 74.75 (+/- 22.85) dB for the right side and 79.25 (+/- 21.91) dB for the left side. Grouped mean ASSR-values (1–2–3 kHz) are 68.85 (+/- 24.20) dB for the right side and 72.07 (+/- 24.20) dB for the left side. When, for ASSR the frequencies 1–2–4 kHz are considered, the grouped mean values become 70.67 (+/- 24.79) dB and 73.01 (+/- 22.89) dB for right and left side, respectively.

As for the specific right and left differences (mean +/- 1 standard error and 1 standard deviation) for each frequency (1, 2, and 3 kHz), CERA versus ASSR, they are compared in ►Fig. 7. The CERA average right and left differences are 4.94 +/- 19.65 dB (1 kHz), 4.78 +/- 18.96 dB (2 kHz), and 3.80 +/- 18.91 dB (3 kHz). While the ASSR average right and left differences are 2.31 +/- 20.57 dB (1 kHz), 2.02 +/- 19.88 dB (2 kHz), and 2.36 (+/- 16.67 dB (3 kHz). Whatever the frequency, the CERA right and left difference exceeds the ASSR right and left difference (n = 156 for each frequency). The analysis of variation (ANOVA) shows no significant frequency effect but, globally, the average CERA right and left difference (4.50 +/- 19.14 dB) is significantly larger than the average ASSR right and left difference (2.23 +/- 19.08 dB). T-test was used for dependent samples, p = 0.003.



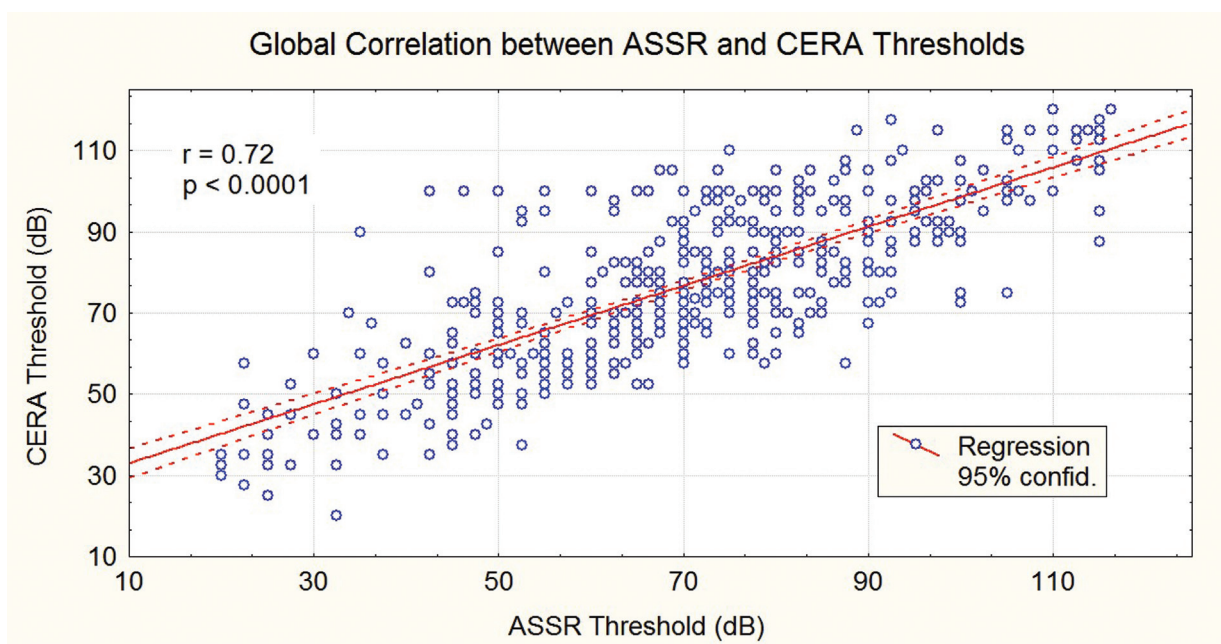
**Fig. 4** As in ►Fig. 3 but for average ASSR thresholds. Again, the average hearing loss increases with frequency, as expected in NIHL ( $p < 0.001$ ). The left threshold is on average always higher than the right one (see ►Table 1).

►Fig. 8 shows the histogram of the right and left threshold differences (dB) as measured (with all frequencies taken together) by CERA and ASSR, respectively. Both distributions are very large, but keep a gaussian shape. The CERA average difference exceeds the ASSR average difference by 2.27 dB.

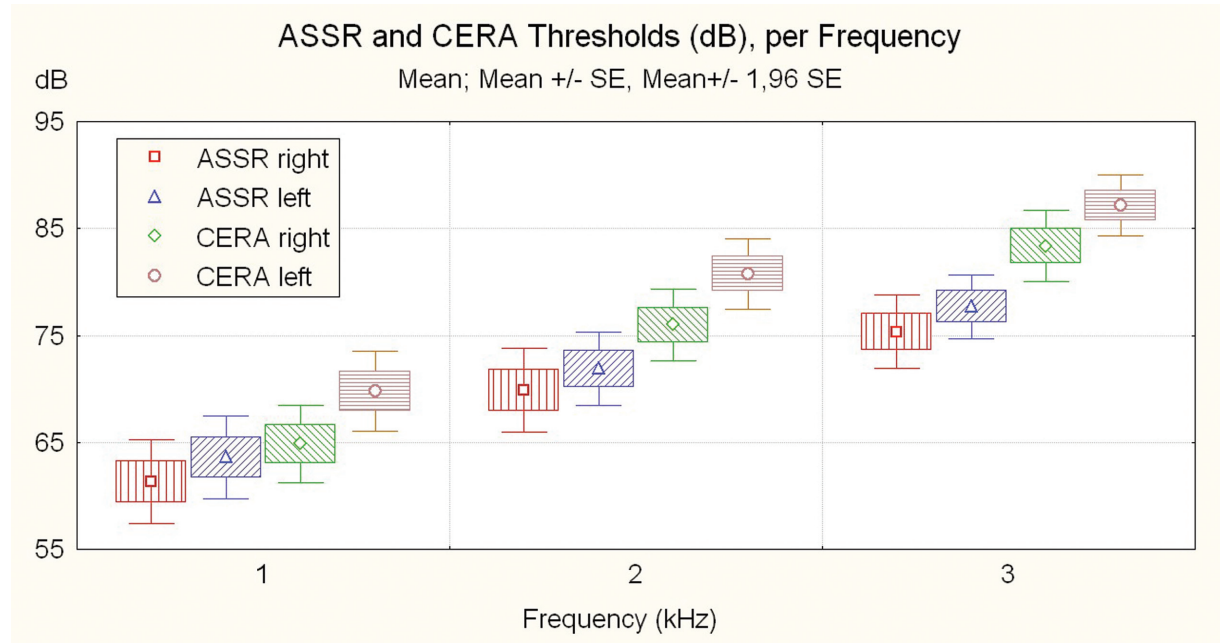
The right and left differences in CERA and ASSR thresholds (with all frequencies taken together) correlate well with each

other (►Fig. 9): the  $r$  value (0.61) is highly significant ( $n = 468$ ).

As can be expected, the computation of partial correlation coefficients does not boost these values. In the case of ASSR, the correlation coefficient between the right and left difference and age becomes  $-0.057$  while controlling for the effect of the degree of hearing loss, and the correlation coefficient



**Fig. 5** Global correlation between the CERA and ASSR thresholds (3 thresholds per ear). The  $r$  value (0.72) is highly significant ( $n = 468$ ).

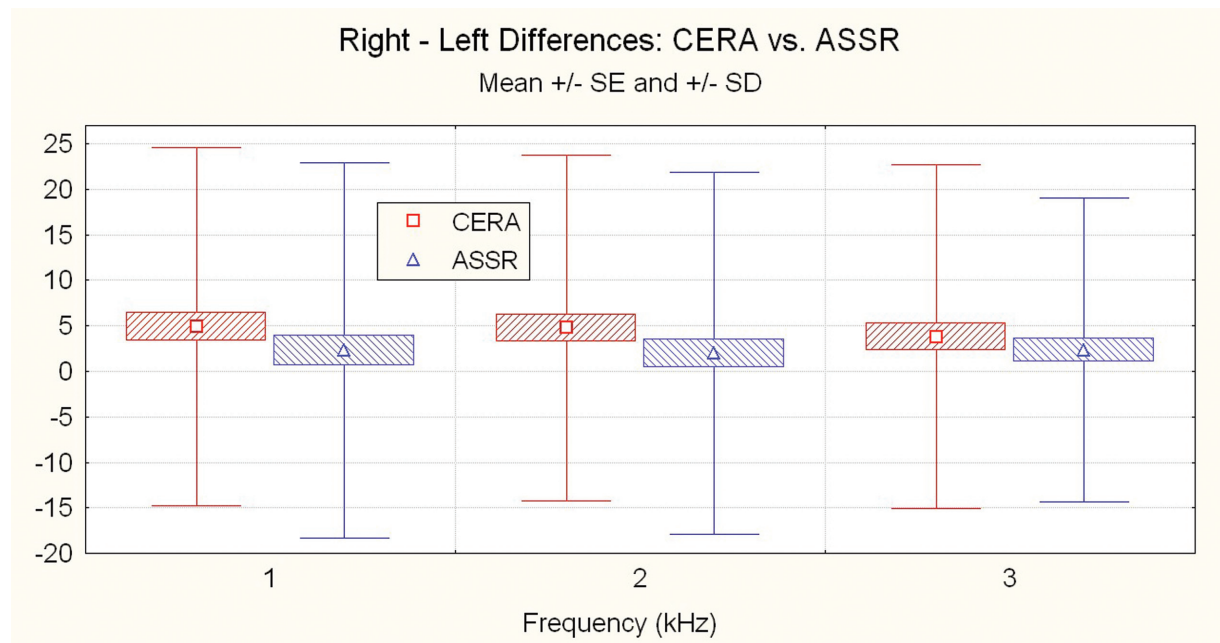


**Fig. 6** Overview of the mean threshold values (+/- 1 and 1.96 standard error) at 1, 2, and 3 kHz for ASSR and CERA, and in the right and left ears respectively. All threshold values increase with frequency. The CERA thresholds exceed ASSR thresholds, and for both techniques the left thresholds are always higher than the right ones (see ► **Table 1**).

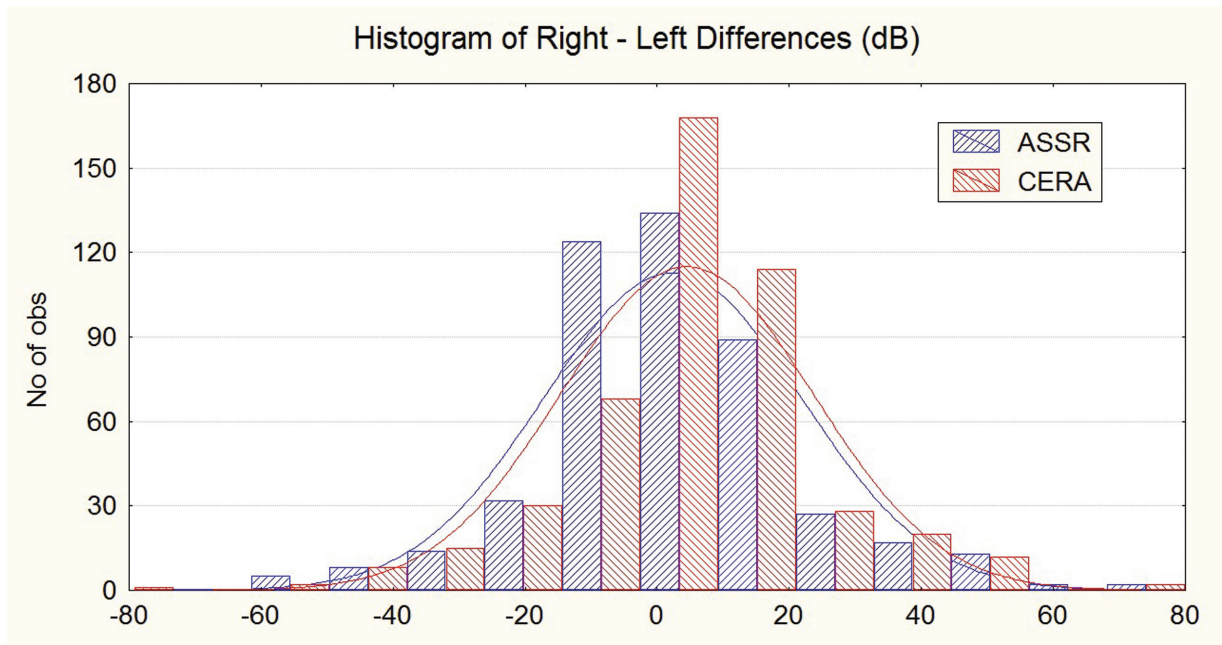
between the right and left difference and the degree of hearing loss becomes -0.102 while controlling for the effect of age.

In the case of CERA, the correlation coefficient between the right and left difference and age becomes 0.016 when

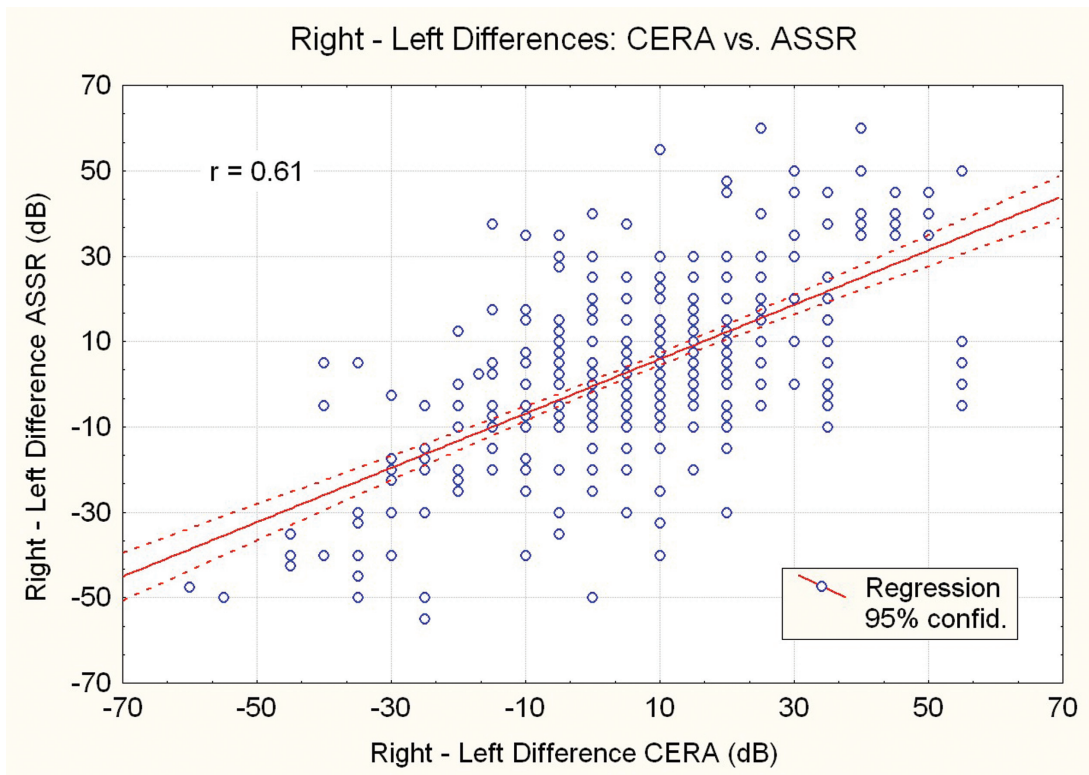
controlling for the effect of the degree of hearing loss, and the correlation coefficient between the right and left difference and the degree of hearing loss is -0.05 when controlling for the effect of age.



**Fig. 7** Mean right-left differences (+/- 1 standard error and 1 standard deviation) for each frequency (1, 2 and 3 kHz), CERA versus ASSR. Whatever the frequency, the CERA difference exceeds the ASSR difference ( $n = 156$  for each frequency). The ANOVA shows no significant frequency-effect, but globally, the average CERA right-left difference (4.50 +/- 19.14 dB) is significantly larger than the average ASSR right-left difference (2.23 +/- 19.08 dB) ( $p = 0.003$ ).



**Fig. 8** Histogram of right–left threshold differences (dB) as measured—all frequencies taken together—by CERA and ASSR, respectively. Both distributions are gaussian. The CERA average difference exceeds the ASSR average difference by 2.27 dB.



**Fig. 9** Correlation between right–left differences in CERA and ASSR thresholds, all frequencies taken together. The  $r$  value (0.61) is highly significant ( $n = 468$ ).



## Discussion

The main innovative outcomes of our study are:

(1) As measured by two different electrophysiological techniques (CERA and ASSR) in a large sample of well documented subjects with moderate to severe NIHL, the average hearing thresholds (1–2–3 kHz) are significantly higher (worse) in the left ear than in the right ear.

(2) The average CERA right and left difference (4.50 +/- 19.14 dB, i.e., 6.02%) is significantly larger than the average ASSR right and left difference (2.23 +/- 19.08 dB, i.e., 3.2%). The CERA average difference exceeds the ASSR average difference by 2.27 dB.

(3) As to the right and left differences, there is no significant effect of frequency.

(4) The right and left differences in CERA and ASSR thresholds (all frequencies taken together) correlate well with each other.

(5) No correlation is observed between right and left differences in hearing thresholds and age, neither for CERA nor for ASSR, even when controlling for the extent of hearing loss.

(6) Similarly, no correlation is observed between right and left differences in hearing thresholds and the degree of hearing loss, neither for CERA nor for ASSR, even when controlling for age.

As to the noise exposure, it is of course impossible to differentiate in our asymmetry findings, specific activities or exposure modes, considering that, when the worker is introducing a compensation claim for NIHL, he has already spent most of his professional career (mean age is 63,4 years), and has in nearly all cases carried various activities with diverse machines, motors, workstations or working benches in different factories or environments, although invariably with a significant and persistent exposure to damaging noise levels (for an average duration of 27 years) as emerges from the detailed report of the engineer. Hence, we have a sample that is truly representative of the generic concept of 'occupational noise exposure' and its consequential moderate to severe NIHL.

As to the observed right and left difference, it seems likely that the true value must be that shown by ASSR (2.23 +/- 19.08 dB, i.e., 3.2%). As mentioned, the CERA average difference exceeds the ASSR average difference by 2.27 dB, which is non negligible and cannot be accounted for by the lower sensitivity of CERA. However, the most plausible explanation is pragmatic: the ASSR technique, that explores both ears simultaneously and is faster, was usually performed first. As to CERA, which is much more time consuming, the right ear was usually tested first. This means that when it came to the left ear, increased parasitic movements and enhanced alertness controls may have reduced the signal-to-noise ratio of the responses, slightly raising the thresholds.

Admitting that the average asymmetry of NIHL is established, competing theories about its causality can be reconsidered, as the reason why the left ear is more susceptible to noise damage is still unclear.<sup>1</sup>

Asymmetry in NIHL could theoretically be caused either by environmental exogenous noise-exposure factors or by endogenous, anatomical or physiological factors.<sup>34,35</sup>

Systematically shielding one ear from the noise source, termed the head shadow effect,<sup>34,35</sup> could be an explanation in specific categories of exposure conditions. Our database did not include military personnel, but included one policeman and 2 workers of a fire weapon factory. Roughly, the head mainly reflects high frequency sound waves, i.e., with a wavelength shorter than the head diameter (0.2 m), thus > 1700 Hz considering a sound velocity of 340 m/s. Lower frequencies bend over or around the head.<sup>36</sup> Below 200 Hz, interaural level differences hardly reach a few dB, although they can increase substantially for lateral sources as the distance decreases below 1 m even at low frequencies, while at 1 kHz interaural level differences vary between 5 and 10 dB as a function of source direction.<sup>37</sup> Above 1 kHz, interaural level differences and their directional dependency continue to increase with frequency.<sup>38</sup> However, no association has been found between the frequency octave bands with the higher levels of noise and the auditory damage frequencies: frequencies with the highest audiometric thresholds do not coincide with the frequency bands the intensity levels of which reach higher values.<sup>7</sup> Actually, we did not find an effect of frequency (1–2–3 kHz) on the right and left difference, but the interaural differences may not be considered negligible.

The head shadow effect could plausibly be related to handedness. However, some studies assessing the effect of handedness on hearing loss did not support the hypothesis.<sup>3,39–41</sup> Information about right- or left-handedness is however missing in our study.

As to a possible effect of frequency on the right and left difference: when NIHL progresses, it first and mainly affects high frequencies. Hence the right and left difference could be expected to be slightly higher at 3 kHz than at 1 kHz, but this effect is probably too subtle to show up in our analysis.

As to the endogenous/physiological factors, a putative / potential protecting effect on the right ear has been investigated by different approaches. A theory incriminating a possibly less sensitive left-sided acoustic-facial reflex does not seem convincing.<sup>1,3,39,42,43</sup> No asymmetry in acoustic reflex thresholds has been demonstrated in subjects with asymmetrical NIHL. Moreover, in humans and animal models, a unilateral paralysis of the stapedius muscle resulted in increased temporary or permanent threshold shift after noise exposure, but this concerned predominantly the lower frequencies.<sup>44,45</sup>

Alternatively, the left ear could somehow be more susceptible to NIHL than the right one, and more adversely affected by noise. Olivocochlear efferents may modulate cochlear nerve excitability, protecting the cochlea from neural damage in acoustic injury and decreasing the risk of permanent noise-induced hearing loss.<sup>46–48</sup>

Otoacoustic emissions (OAEs) reflect activity from active mechanisms of the outer hair cells that amplify acoustic energy in the cochlea. OAEs are modulated by the medial olivocochlear efferent system in the brainstem.<sup>49</sup> By quantifying spontaneous otoacoustic emissions, Khalifa and Collet<sup>42</sup>

observed that the medial olivocochlear system, that contralaterally attenuates evoked otoacoustic emissions, appears to be more functional in the right ear than in the left ear. Efferent neurons of this pathway synapse with outer hair cells and cause hyperpolarization. This reduction in resting membrane potential decreases outer hair cell activity and vibration of the basilar membrane.<sup>1,50</sup> The medial efferent system may initiate or regulate a slow contraction of the outer hair cells.<sup>51</sup> This implies that the right ear may be better protected against noise damage than the left ear due to stronger efferent inhibition. The medial efferent system has been found to be more effective in the right than left ear in right-handers, while functioning symmetrically in left-handers.<sup>52</sup>

Furthermore, Bidelman and Bhagat<sup>53</sup> found that modulation of peripheral cochlear processing (and the possibly resulting protective effect), is specifically stronger (in the right ear) for high frequency cochlear regions (basal cochlea). A stronger protective effect of the olivocochlear efference on the higher frequencies in the right ear should also – if important enough – be reflected in our right and left differences, but this effect seems too small or masked.

Interestingly, it has also been reported that tinnitus is much more common in the left ear than in the right ear.<sup>54</sup>

In summary, the centrifugal olivocochlear pathways can have a protecting effect on the cochlea from loud sounds damage. However, the question of laterality remains complex. As emphasized by Rajan,<sup>55</sup> the cochlea receives a dual-component efferent innervation: on the one hand, the lateral olivocochlear system, almost exclusively from only the ipsilateral superior olivary nucleus, terminates on dendrites of afferent neurons (not on the outer hair cells). On the other hand, the medial olivocochlear system, originating from ipsilateral (uncrossed) and contralateral (crossed) periolivary nuclei, terminates on outer hair cells. The activity of the uncrossed medial olivocochlear efferent pathway has been shown to be more effective in the right ear than in the left ear. Philibert et al.<sup>56</sup> confirmed the uncrossed pathway asymmetry and observed a reverse asymmetry in the crossed pathway, hence a left ear advantage.

Our results provide clear arguments neither in favor of the differential exposure theory nor in favor of a neurophysiological protective effect. Both of them seem likely to intervene. Our two electrophysiological approaches just confirm each other as to the asymmetry. However, without shedding new light on a possible central process. Only the invariance of the right and left difference (for frequency, age, and degree of hearing loss) is intriguing and might argue for the intervention of an invariant mechanical factor.

## Conclusion

In occupational NIHL, the CERA and ASSR measurements confirm that there is an actual average right and left differ-

ence of approximately 2.23 dB (3.2%). A differential exposure as well as an efferent olivocochlear protective effect are likely to account for this asymmetry.

## Ethical Statement

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional guidelines on human experimentation (in this case audiological investigations) and with the Helsinki Declaration of 1975, as revised in 2008.

## Funding

The author(s) received no financial support for the research.

## Conflict of Interest

The authors have no conflict of interests to declare.

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