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Magnitude of the contralateral efferent olivocochlear effect as a function of the frequency

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ABSTRACT

Background: The activation of the medial olivocochlear reflex reduces the cochlear gain, which is manifested perceptually as decreased auditory sensitivity. However, it has remained unclear whether the extent of this suppression varies according to the cochlear region involved. Here we aim to assess the magnitude of contralateral efferent suppression across human cochlea, at low levels, and its impact on hearing sensitivity.

Methods: Assuming that acoustic stimulation activates the contralateral medial olivocochlear reflex, we evaluated the magnitude of the suppressive effect as a function of frequency in 17 subjects with normal hearing. Absolute thresholds were measured for burst tones of various durations (10, 100, and 500 ms) and frequencies (250, 500, 1000, 4000, and 8000 Hz) in the presence or absence of contralateral white noise at 60 dB SPL.

Results: We found that contralateral noise raised the absolute threshold for the burst tones evaluated. The effect was greater at lower than higher frequencies (3.85 dB at 250 Hz vs. 2.22 dB at 8000 Hz).

Conclusions: Our findings suggest that in humans, the magnitude of this suppression varies according to the cochlear region stimulated, with a greater effect towards the apex (lower frequencies) than the base (higher frequencies) of the cochlea.

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1. Introduction

The efferent auditory system allows the brain to modulate the cochlear response, primarily via the medial olivocochlear system (MOC). In mammals, the effect of MOC fibers activation has been studied through electrical stimulation in the floor of the fourth ventricle and/or activating the MOC reflex, through stimulation with an ipsi or contralateral acoustics stimulation (Chambers et al., 2012; Robertson and Gummer, 1985). Regardless of the stimulation mechanism, the main effect of MOC fibers activation is a reduction in the gain of the cochlear amplifier (Guinan and Cooper 2008; Cooper and Guinan 2006; Murugasu and Russell 1996), in a level-dependent way. It is greater at low levels and decreases as the measurement level increases.

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Studies in humans have demonstrated a suppression of otoacoustic emissions (OAE) in the presence of a ipsilateral (IAS) and/or contralateral acoustic stimulation (CAS), presumably due to activation of the medial olivocochlear reflex (MOCR). This suppressive effect is the electroacoustic correlate of the decreased cochlear gain observed in physiological studies of other animals. While OAE are produced by outer hair cells and therefore reflect cochlear function, these signals are not necessarily indicative of the perceptual function.

At the perceptual level, previous research has measured the effect of acoustics stimulation (ipsi and/or contralateral) on auditory properties such as frequency (Aguilar et al., 2013; Jennings et al., 2009; Kawase et al., 2000; Quaranta et al., 2005; Vinay and Moore, 2008; Wicher and Moore, 2014) or compression (Fletcher et al., 2016; Jennings et al., 2009; Krull and Strickland, 2008; Yasin et al., 2014). All these perceptual results were possible to explain by the cochlear gain reduction model, due to the reflex activation of the ipsi or contralateral medial olivocochlear fibers.

Although it is widely accepted that MOCR activation has a suppressive effect on the cochlea, there are important aspects of this reflex in humans that we must know in more detail: Does the magnitude of the efferent effect vary across the human cochlea? This study aims to add information on that line. Especially, whether the magnitude of the contralateral MOCR effect varies according to the cochlear region at low levels, and its impact on hearing sensitivity.

Previous studies have partially elucidated these questions. Using stimulus frequency otoacoustic emissions (SFOAE) Lilaonitkul and Guinan (2009) suggest a greater efferent effect at the apex (500 and 1000 Hz, than at the base (4000 Hz) (see Fig. 3, in the cited research). Consistent with this result, using the perceptual technique of temporal masking curves (TMC) Aguilar et al. (2013) observed a greater effect of MOCR on cochlear compression at the apex (500 Hz) than at the base (4000 Hz). Although both studies are qualitatively consistent, they were not designed to provide precise data (in dB) about the magnitude of the reduction in cochlear gain and its effect on hearing sensitivity.

Kawase et al. (2003) explores the effect of broadband noise on brief (50 ms) tone thresholds for a wide frequency range (500–8000 Hz). The main result observed is a greater effect at low-mid frequencies and less effect at high frequencies. In a similar approach, Aguilar et al. (2015) measured the absolute thresholds for burst tones (500 or 4000 Hz) as a function of duration (ranging from 10 to 500 ms) in the presence or absence of CAS. This design allowed the authors to approximate the magnitude of efferent suppression of the basilar membrane at various levels near the absolute threshold. Assuming that contralateral acoustic stimulation activates MOCR, the main findings of this study can be summarized as follows: i) MOCR activation increased the auditory threshold by an average of approximately 1.4 dB for both frequencies. The effect was slightly greater at 4000 than 500 Hz, but the difference was not statistically significant. ii) For both frequencies, the suppressive effect was greater for longer tones. Nogueira et al. (2019) evaluated the effect of contralateral suppression on auditory threshold in single-sided deaf cochlear implant users, using 10- or 200-ms tones at 500 or 4000 Hz. To evoke the MOCR, the authors presented pulse trains on 16 sequentially-stimulated electrodes at 843 Hz to produce contralateral broadband electrical stimulation (CBES). The authors observed that the CBES increase the auditory threshold. This effect was greater for 500 than at 4000 Hz, and was significant for 10-ms 500-Hz tones, in which case the threshold was elevated by 1.2 or 2.2 dB with CBES equivalent to 50 or 60 dB, respectively.

Under the reasonable assumption that contralateral acoustic stimulation activates the contralateral medial olivocochlear reflex, here we measure the effect of contralateral white noise (CWN) on absolute threshold for burst tones over a wide frequency range (250–8000 Hz). This information will allow us to infer the magnitude of the contralateral MOCR along the human cochlea. In order to evaluate a possible level-dependent effect, tones of different durations (10–500 ms) were measured.

The absolute threshold of a tone varies depending on its duration. When the duration of a tone is increased, the perceptual threshold decreases. The slope varies as a function of frequency (Watson and Gengel, 1969). Regardless of the cause (discussed in (Aguilar et al., 2015), the auditory threshold of a tone, at fixed frequency, it depends on the interaction of at least two components: The duration of the tone and the excitation level of the auditory receptor, in a range up to 500 ms approximately (Watson and Gengel 1969; Viemeister and Wakefield 1991). Therefore, if we measure the effect of a CAS on the hearing threshold of a tone at different durations, we can evaluate the effect of the MOCR as a function of cochlear excitation at low levels. If there were a

perceptual correlate of the level-dependence effect described in mammals (Cooper and Guinan, 2006), we would expect a greater suppressive effect in longer duration tones.

2. Materials and methods

2.1. Stimuli

Absolute thresholds for burst tones were measured in the presence or absence of CWN, as prior studies have shown that this type of noise is capable of evoking the MOCR (Lisowska et al., 2002). The burst tones had frequencies of 250, 500, 1000, 4000, or 8000 Hz and durations of 10, 100, or 500 ms, with 5-ms cosine onset and offset ramps. The CWN was presented at a fixed level of 60 dB SPL to ensure activation of the MOCR without activating the middle ear muscle (MEM) reflex (Aguilar et al., 2013, 2015; Lopez-Poveda et al., 2013). The CWN was presented for 1000 ms, beginning 400 ms before the onset of the burst tone. This duration is sufficient to evoke the MOCR, given that this reflex is active by 330 ms after the onset of the elicitor (Backus and Guinan, 2006).

2.2. Procedures

The data collection procedures were performed according to Aguilar et al., (2015). The absolute thresholds were measured using a two-alternative forced choice paradigm (2AFC) with visual reinforcement. Two consecutive visual stimuli were presented, only one of which was paired with a probe tone. The probe tone was randomly paired with either the first or second visual stimulus. CWN was presented in the contralateral ear with both visual stimuli. The interval between the CWN and test tone was 400 ms. Participants were instructed to identify the visual stimulus that was paired with the tone, by pressing a key on the computer key board. The intensity of the tone varied according to an adaptive procedure, in which the level was lowered after two hits or increased after one miss (known as the “1 up 2 down” rule). The absolute threshold was defined as the tone intensity that produced a 71% hit rate on the psychometric function (Levitt, 1971). Intensity was adjusted by 6 dB per trial until the third hit, and then by 2 dB per trial. 12 level reversals were measured. The threshold was estimated as the mean of the tone levels of the last 10 reversals. Measurements that exceeded 6 dB standard deviation were discarded. Three valid threshold measurements were obtained for each condition, and the average of the three measurements was used as the absolute threshold. If the standard deviation of the three measurements was greater than 6 dB, additional measurements were performed and included in the average. Therefore, each subject completed thirty valid measurement conditions (five frequencies, three probe tone durations, in the presence and absence of CWN), which were repeated at least three times. In order to become familiar with the technique, all volunteers performed a threshold measurement at any frequencies for a probe tone duration of 500 ms. This measurement was not considered in the analysis.

The measurements were organized considering a period of 10–15 min of rest every three measurements.

To avoid a possible asymmetry in the magnitude of the MOCR between ears, threshold measurements were performed only in the right ear, while contralateral acoustic stimulation was present in the left ear.

The measurements were performed in a soundproof booth with a MOTU Audio Express sound card. The stimuli were generated digitally using “Audiolab” script, designed in the Auditory Computation and Psychoacoustics Laboratory directed by Prof. Enrique López-Poveda (University of Salamanca), in the MATLAB environment and presented via Etymotic ER-2 headphones. These

insert phones were designed to deliver a flat frequency response at the eardrum with an interaural attenuation of +70 dB, and were calibrated at 1 kHz and the measured sensitivity was applied to all other stimuli, using a Larsson Davis System 824.

The experimental procedures were approved by the University of Chile Human Research Ethics Committee and carried out at the Audiology and Auditory Perception Laboratory, in the Department of Medical Technology.

2.3. Subjects

A total of 17 normal hearing volunteers completed testing (10 male and 7 female), ranged from 18 to 25 years old, and they were recruited from the university campus. Subjects were volunteers and were not paid for their services. Before participating in the study, subjects signed an informed consent form. Prior to testing, subjects were evaluated to ensure a normal tympanogram and clinical audiometric threshold below or equal to a 20 dB hearing level, at all frequencies studied (125–8000 Hz) in both ears.

3. Results

Fig. 1 shows the average absolute thresholds for the burst tones of various durations and frequencies with and without CWN. As expected, auditory thresholds increased as the duration of the test tone was shortened. This effect occurred in both the presence and absence of CWN. When the thresholds are plotted against test tone duration, the curve is steeper for low vs. high frequencies in the absence of CWN, consistent with previous findings (Aguilar et al., 2015; Nogueira et al., 2019; Watson and Gengel, 1969).

3.1. Effect of CWN on absolute thresholds

The main effect observed was an increase in absolute threshold in the presence of contralateral stimulation (Fig. 1).

Fig. 2 illustrates the average effect of CWN, across probe durations, as function of frequency. There is a clear trend reflecting a

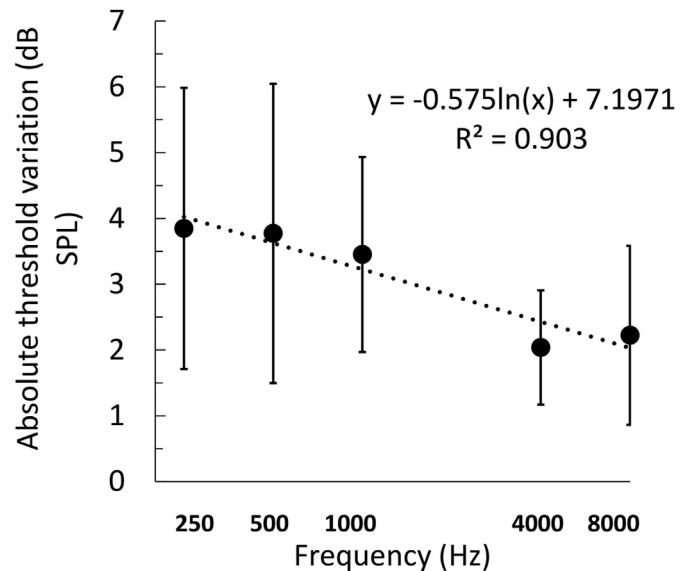


Fig. 2. Magnitude of MOCR efferent effect activation (dB). Mean threshold elevation across frequency. Error bars illustrate one standard deviation.

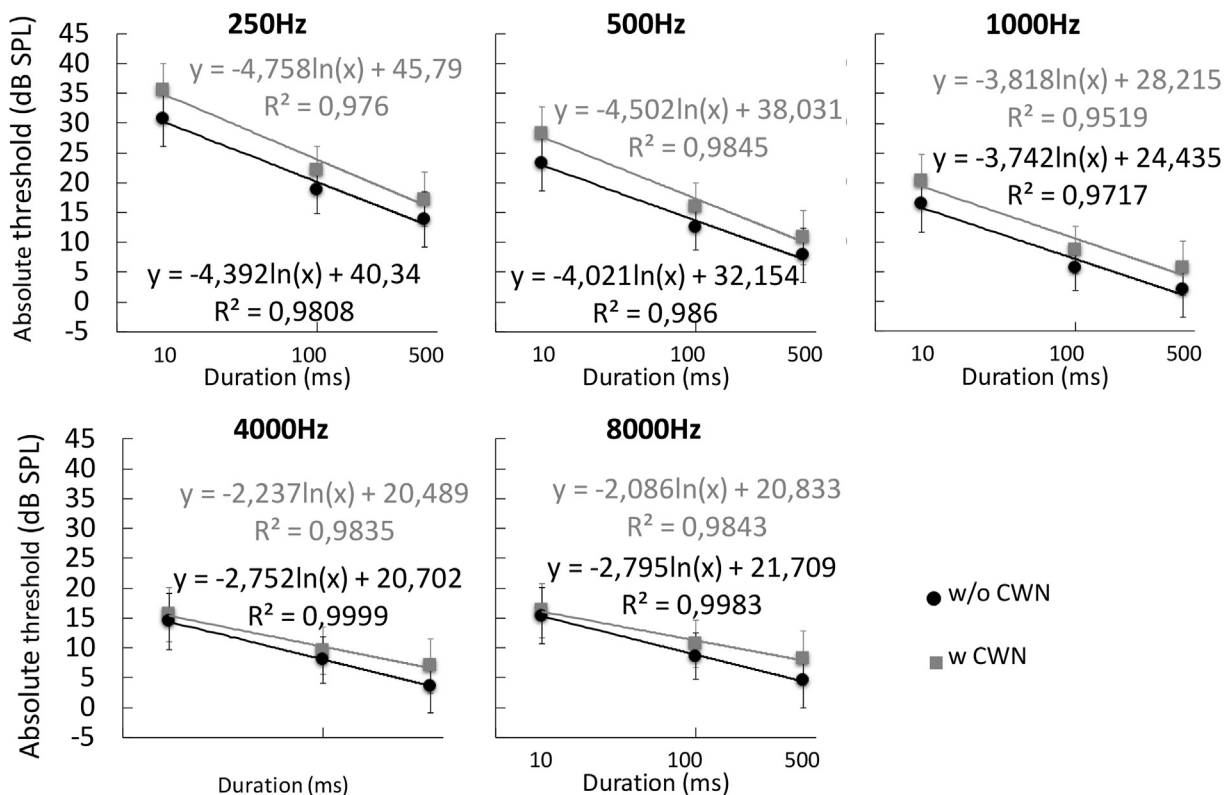


Fig. 1. The mean effect of contralateral white noise on absolute detection thresholds for burst tones of different durations. Each curve is for a different frequency (250–8000 Hz). Symbols represent mean thresholds in the absence ('w/o CWN', black circle) and in the presence ('w CWN', gray square) of a CWN. Lines illustrate least-squares fits to the data using the logarithmic functions given next to the data. Error bars illustrate one standard deviation.

decreasing effect of CWN as the frequency of the test tone increases, with the greatest effect at 250 Hz (3.85 dB) and the smallest effect at 8000 Hz (2.22 dB).

The average threshold graphs (Fig. 1) show that the effect of contralateral stimulation is markedly greater for long (500 ms) than short tones (10 ms) at frequencies of 4000 and 8000 Hz. On the other hand, the effect of contralateral noise is slightly greater for short (10 ms) than long (500 ms) tones at frequencies of 250 and 500 Hz.

To determine whether the effects of CWN condition, test tone duration, and test tone frequency on absolute threshold were significant, and to evaluate the interactions among these effects, results were analyzed using a three-way repeated measures analysis of variance (ANOVA). The effect of CWN was statistically significant ($F(1, 16) = 174.7, p \leq 0.01$), with a higher absolute threshold in the presence vs. absence of the noise. As expected, both, the frequency ($F(2.6, 41.9) = 45.76, p \leq 0.01$) and probe duration ($F(1.2, 20.17) = 745.6, p \leq 0.01$) have a significant effect on the tone threshold.

The interaction between CWN condition and test tone frequency was also significant ($F(2.46, 39.41) = 5.21, p \leq 0.01$); the frequency-dependent effect described in Fig. 2 is statistically significant.

As inferred from Fig. 1, the slope of the curve for threshold vs. test tone duration was steeper for low vs. high frequency test tones. However, these interactions behaved differently in the presence vs. the absence of CWN. For frequencies of 250 and 500 Hz, the slope of the curve is slightly steeper in the presence vs. absence of CWN. Conversely, at 4000 and 8000 Hz, the slope is steeper in the absence vs. presence of CWN. At a frequency of 1000 Hz, the curves in the presence and absence of CWN are nearly parallel.

The statistical significance of the differences between the slopes was analyzed using a student's *t*-test (two tailed, paired *t*-test). The difference between the slopes for the conditions with and without CWN was significant ($p \geq 0.05$) at test tone frequencies of 500, 4000, and 8000 Hz.

4. Discussion

The aim of this study was to assess whether the magnitude of the contralateral MOCR varies according to the region of the human cochlea stimulated, at low levels. Assuming that CAS is able to evoke the MOCR, we compared the absolute thresholds for burst tones of various durations (10–500 ms) and frequencies (250–8000 Hz). In the absence of CAS, the threshold decreased as test tone duration increased, as expected. The slope of the curve for threshold vs. probe tone duration was more pronounced for lower vs. higher frequencies, also consistent with prior studies (Aguilar et al., 2015; Nogueira et al., 2019; Watson and Gengel, 1969).

CWN increased the detection threshold by an average of 3.06 dB across the frequencies studied. This finding is consistent with a reduction in the gain of the cochlear amplifier, an effect that has been widely reported in humans and other mammals (see (Lopez-Poveda, 2018)). Furthermore, as observed in Aguilar et al. (2015), the average effect of CWN was greater for longer vs. shorter probe tones.

As shown in Fig. 2, there was also a clear decrease in the effect of the CWN as the probe tone frequency increased, from 3.85 dB at 250 Hz to 2.22 dB at 8000 Hz. These results are qualitatively similar to those reported by Lilaonitkul and Guinan (2009). These authors measured the effect of the contralateral MOCR on stimulus-frequency otoacoustic emissions (SFOAE) in humans at 500, 1000, and 4000 Hz and found a greater effect of the MOCR for lower vs. higher probe tone frequencies. In terms of perceptual measurements, Aguilar et al. (2013) reported a greater suppressive effect of the contralateral MOCR on psychophysical tuning curves (PTC) for

frequencies of 500 vs. 4000 Hz. Moreover, Nogueira et al. (2019) found a greater effect on sensitivity to a short tone (10 ms) at frequencies of 500 vs. 4000 Hz. Using a similar protocol to the one used here, Aguilar et al. (2015) found no significant difference between frequencies of 500 and 4000 Hz. This apparent discrepancy may be attributable to different methodologies, as the Aguilar et al. study tested a smaller number of subjects and had a slightly older sample than the present study (29 vs. 21 years of age). Kawase et al. (2003) found a greater suppressive effect for middle (1000 and 2000 Hz) than low (25 or 500 Hz) or high (4000 or 8000 Hz) frequencies in the presence of 60 dB SPL broadband noise. It is difficult to identify the source this discrepancy, due to significant differences in stimulus and measurement conditions between the present study and the Kawase protocol. One critical factor may be the type of headphones used. This study used insert headphones (Etymotic ER-2), but the equipment used in Kawase et al. (2003) was not reported. If supra-aural headphones were used, the nominal interaural attenuation may have affected the auditory thresholds considerably through masking. This detail would explain the size of the reported effect (approximately 8 dB at 2000 Hz), and the marked elevation of the thresholds when the contralateral stimulus exceeds 50 dB, that matches the typical nominal interaural attenuation levels reported for supra-aural headphones. A second methodological difference that could explain these differences is the eliciting stimulus of the MOCR. We used a white noise, while Kawase et al. (2003) used narrow band noise (NBN), possibly centered on probe tone frequency (not specified). Finally, Kawase et al. (2003) five ears (four subjects) were studied, possibly indistinctly right or left (not specified). Unlike, we evaluate only right ears, given the possibility of the existence of an advantage of the right ear indicated in the methodology.

Our finding that the magnitude of the effect varied according to the frequency of the test tone suggests that the contralateral efferent olivocochlear effect is more robust near the apex than the base of the human cochlea. The density of MOC innervation along the human cochlea is largely unknown; however, we know that there is a tonotopic gradient of olivocochlear innervation in other mammals. In mice, for example, MOC innervation is densest in the medial cochlea (Maison et al., 2003). On the other hand, MOC innervation is denser in the apical vs. the basal zone of the cochlea in chinchillas, who have a frequency response similar to that of humans (Iurato et al., 1978).

We know that the ears do not function independently of one another. On the contrary, auditory function is modulated by efferent control, which is dependent on the listening environment. In recent years, researchers have explored the use of biologically-inspired auditory models that include efferent control in the design of cochlear implants (Lopez-Poveda et al., 2016, 2017, 2019, 2020; Lopez-Poveda and Eustaquio-Martín, 2018), an approach that offers the potential to significantly improve these devices. This study contributes functional information on the relationship between the magnitude of the MOCR and the region of the human cochlea stimulated that can be incorporated into new models of efferent control of the cochlea.

A possible limitation of this study is that the increase in thresholds due to contralateral acoustic stimulation is due to the central masking phenomenon (Zwislocki, 1972) and not to the contralateral MOCR. However, central masking is currently under discussion based on the report Smith et al. (2000), who evidenced an increase in perceptual tonal thresholds in macaques as a result of contralateral acoustic stimulation (60 dB SPL, two active noise centered at probe tone). However, this increase practically disappears when the MOC fibers are sectioned, which would reinforce the idea that the increase in the perceptual threshold is due to a reduction in cochlear gain and not to the “central masking”.

The perceptual manifestations of MOCR activation could depend on the non-linear properties of the auditory filters. In this sense, the gain, compression and bandwidth of the studied auditory filter could be related to the magnitude of the MOCR. In fact, Pearson's correlation analysis between the average effect of CWN, across probe durations with the absolute threshold across probe durations, for each frequency studied reflects a trend towards negative correlations. Being significant (bilateral) at 4000 Hz ($r = -0.56$, $(p) = 0.018$). That is, subjects with lower absolute thresholds, had a greater magnitude of the efferent effect. This phenomenon could also occur in the contralateral ear, where the eliciting sound could activate the MOCR to a greater extent in subjects with lower hearing thresholds. We cannot verify this with our approach because thresholds were not obtained with the adaptive method in the left ear. Future research, specially configured for this purpose, should determine the impact of the non-linear properties of the auditory filters on the magnitude of the MOCR.

5. Conclusion

Our main findings can be summarized as follows:

- 1) The absolute threshold for burst tones increases when contralateral white noise is presented at 60 dB SPL to elicit the medial olivocochlear reflex (MOCR). That is, MOCR activation decreases auditory sensitivity and therefore reduces cochlear gain.
- 2) The suppressive efferent effect of the MOCR is greater for lower- vs. higher-frequency test tones (3.85 dB at 250 Hz, 3.77 dB at 500 Hz, 3.45 dB at 1000 Hz, 2.04 dB at 4000 Hz, and 2.22 dB at 8000 Hz). This finding suggests that the magnitude of the contralateral medial olivocochlear reflex may vary according to the cochlear region stimulated, with a greater affect towards the apex than the base of the cochlea.

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