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Medial olivocochlear reflex effects on synchronized spontaneous otoacoustic emissions

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Abstract: This study characterized medial olivocochlear (MOC) reflex activity on synchronized spontaneous otoacoustic emissions (SSOAEs) as compared to transient-evoked otoacoustic emissions (TEOAEs) in normal-hearing adults. Using two time windows, changes in TEOAE and SSOAE magnitude and phase due to a MOC reflex elicitor were quantified from 1 to 4 kHz. In lower frequency bands, changes in TEOAE and SSOAE magnitude were significantly correlated and were significantly larger for SSOAEs. Changes in TEOAE and SSOAE phase were not significantly different, nor were they significantly correlated. The larger effects on SSOAE magnitude may improve the sensitivity for detecting the MOC reflex.

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1. Introduction

The medial olivocochlear (MOC) reflex modifies activity of the outer hair cells to enhance signal detection in noise and protect the auditory system from acoustic trauma [reviewed in Lopez-Poveda (2018)]. Measurements of the MOC reflex provide insight into auditory mechanics and may also hold clinical utility such as identifying individual risk for noise-induced hearing loss (Maison and Liberman, 2000). One method of measuring the MOC reflex utilizes transient-evoked otoacoustic emissions (TEOAEs), sounds generated as a byproduct of outer hair cell motility that are elicited by brief stimuli (Kemp, 1978). TEOAE amplitudes are typically inhibited by MOC reflex activation from a contralateral elicitor such as broadband noise (Collet *et al.*, 1990). TEOAE-based measurements of the MOC reflex focus on the response occurring within 20 ms following the onset of the transient stimulus. Transient stimuli can also elicit synchronized spontaneous otoacoustic emissions (SSOAEs), which are emissions generated by the same linear coherent reflection mechanism as TEOAEs (Shera, 2003) but persist for a longer duration, such as >20 ms (Keefe, 2012). SSOAEs are highly prevalent in normal-hearing listeners, with estimates ranging from 70% to 100% (Sisto *et al.*, 2001; Jedrzejczak *et al.*, 2008; Keefe, 2012; Lewis, 2018).

The presence of SSOAEs may provide advantages as well as challenges for TEOAE-based measurements of the MOC reflex. Lewis (2018) and Jedrzejczak *et al.* (2020) recently demonstrated that SSOAEs can increase the signal-to-noise ratio (SNR) of TEOAEs, which allows for more sensitive detection of MOC-induced changes in TEOAE amplitude (MOC effects) relative to when SSOAEs are absent. However, SSOAEs could complicate measures of the middle ear muscle (MEM) reflex that are used in studies of the MOC. It is desirable to avoid MEM reflex activation when assessing the MOC reflex because the MEM reflex can alter TEOAE amplitudes that could be misinterpreted as being caused by the MOC reflex (Guinan *et al.*, 2003). MEM reflex activation can be detected as a change in the TEOAE-evoking stimulus amplitude in the presence of a contralateral elicitor due to an MEM-reflex-induced change in middle ear impedance. If an SSOAE overlaps in time with the following stimulus, and if the SSOAE is sufficiently inhibited by the contralateral elicitor, this could be exhibited as a change in ear-canal stimulus amplitude, which could lead to an erroneous conclusion that the MOC reflex measurement was contaminated by MEM reflex activity (Marks and Siegel, 2017; Mertes, 2020).

Previous reports have shown that a contralateral MOC reflex elicitor can inhibit the amplitude of SSOAEs, only example results were presented (Goodman *et al.*, 2018; Mertes, 2018). The purposes of the current study were to quantify MOC-induced changes in SSOAE magnitude and phase across frequencies and to examine the associations with MOC effects on

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TEOAEs. This study was exploratory in nature and represents a step toward determining the impact that SSOAEs may have on TEOAE-based measurements of the MOC reflex.

2. Methods

The research protocol was approved by the University of Illinois at Urbana-Champaign's Institutional Review Board and written informed consent was obtained from all participants. Participants consisted of 26 adults (25 females; mean age ± 1 SD $= 21.54 \pm 3.48$ years). All participants had a negative history of otologic pathology, an unremarkable otoscopic examination, air- and bone-conduction thresholds ≤ 20 dB hearing level (HL) at octave frequencies from 0.25 to 8 kHz bilaterally, type A 0.226 kHz tympanograms bilaterally, and measurable TEOAEs (SNR >6 dB from 1 to 4 kHz) in the right ear in response to 2400 clicks presented at 65 dB peak sound pressure level (pSPL) and at a rate of 20/s (Mertes, 2018).

Testing took place in a single-walled sound-treated booth. The recording setup consisted of a Microsoft Windows–based PC running MATLAB version 2018a (The MathWorks, Inc.) and ARLas recording software (Goodman, 2016) interfacing with a 24-bit Babyface Pro audio interface (RME), an ER-10C probe microphone with 20 dB of preamplifier gain (Etyōmtic Research), and an ER-2 insert earphone (Etyōmtic Research). A sampling rate of 44.1 kHz was used for stimulus generation and response recording.

Measurements were adapted from those described in Mertes (2018). Participants were seated in a recliner, instructed to remain still and quiet, and watched a closed-captioned silent video of their choice on a tablet computer. Clicks for eliciting TEOAEs were presented through the ER-10C probe to the right ear and consisted of 22.7-μs pulses presented at a rate of 20/s and at a level of 65 dB pSPL as calibrated in each participant's ear canal. Contralateral acoustic stimulation (CAS) for eliciting the MOC reflex was presented to the left ear through the ER-2 earphone and consisted of broadband Gaussian noise with an electrical bandwidth of 0–22.05 kHz and a root-mean-square (RMS) level of 60 dB sound pressure level (SPL) as calibrated in a 2-cc coupler. Measurements consisted of alternating between 4000 ms of clicks presented without CAS (CAS−), 500 ms of CAS alone to allow for full onset of the MOC reflex (Backus and Guinan, 2006), 4000 ms of clicks presented with CAS (CAS+), and ending with 500 ms of silence to allow for full offset of the MOC reflex (Backus and Guinan, 2006). This sequence was repeated 30 times resulting in 2400 recorded sweeps (individual stimulus presentations) each for the CAS− and CAS+ conditions.

Waveforms were time windowed so that from hereafter, time zero refers to the location of the stimulus peak. Waveforms with an RMS amplitude exceeding 1.5 times the interquartile range (IQR) of all RMS amplitudes within a participant were discarded. A check of MEM reflex activation was implemented using the critical difference method described in Mertes (2020) that compares the change in ear-canal stimulus amplitude between CAS− and CAS+ conditions in an individual to the distribution of changes in stimulus amplitude within the CAS− condition. In an individual participant, if this difference exceeded the 95th percentile critical difference, this was interpreted as probable MEM reflex activation.

MOC effects were assessed by analyzing the recorded waveforms in two time windows as used in Mertes (2018): 8–18 ms (TEOAE window) and 34–44 ms (SSOAE window). The TEOAE window is a common window for analyzing MOC reflex effects on TEOAEs because effects are largest in this window (e.g., Hood *et al.*, 1996) and the SSOAE window is extended far enough to not contain TEOAEs (Mertes, 2018).[1] The 1-ms portion preceding and following these window durations were ramped on and off with a Hann window to reduce splatter in the frequency domain analysis. Waveforms were bandpass filtered with a Hann-window-based finite impulse response digital filter with cutoff frequencies of 0.5 and 6.0 kHz and a filter order of 256. To obtain an estimate of the TEOAE and SSOAE signals and noise floors, odd- and even-numbered waveforms were stored in two separate buffers, then the signal was estimated as the mean of the two buffers and the noise floor was estimated as the mean of the difference of the two buffers. A 1024-point fast Fourier transform (FFT) was computed on the mean signal and noise floor waveforms for the two analysis windows. The FFT magnitude (in dB SPL) and unwrapped phase (in cycles) were each averaged in five 1/2-octave bands. The center frequencies (with bandwidths in parentheses) were 1 (0.84–1.19), 1.4 (1.19–1.68), 2 (1.68–2.38), 2.8 (2.38–3.36), and 4 (3.36–4.76) kHz. The analysis bandwidths were identical for the TEOAE and SSOAE windows. At each frequency band, a participant's results were included in the analysis if the SNR averaged across frequencies within that band exceeded 9 dB (Marshall *et al.*, 2014) for the CAS− condition.[2] The MOC effect was quantified as the decibel difference in signal magnitude between the CAS− and CAS+ conditions, where positive values indicated inhibition and larger values indicated a stronger MOC reflex. Phase shifts were quantified as the difference in mean phase between the CAS− and CAS+ conditions, where positive values indicated a phase

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lead in the presence of CAS. Responses were verified to be absent in a 2-cc coupler. This report focuses on magnitude and phase changes at the group level, with future directions to include analyses at the individual participant level.

3. Results

For the MEM reflex check, no participants exceeded the 95th percentile critical difference of ±0.081 dB. The median change in stimulus amplitude with CAS was 0.006 dB (range = −0.039 to 0.033 dB). These results suggest that the contralateral elicitor did not activate the MEM reflex.

The number of participants exhibiting SSOAEs in at least one frequency band for the CAS− condition was 18 (69.23%). When collapsed across frequency, the median TEOAE SNR was 21.71 dB for participants with SSOAEs and 14.43 dB for participants without SSOAEs. Figure 1 shows examples of the magnitude spectra obtained in a participant with SSOAEs (top row) and without SSOAEs (bottom row). In both cases, participants had robust TEOAEs from 1 to 4 kHz that decreased in magnitude in CAS+. The participant shown in the top row had prominent peaks in the spectrum obtained in the SSOAE window at 1.55 and 2.46 kHz, with a smaller peak at 3.40 kHz. The SSOAE magnitudes decreased in CAS+. Conversely, the participant shown in the bottom row had signal magnitudes that fell into the noise floor in the SSOAE window.

Table 1 displays descriptive statistics for the group results obtained in CAS− and CAS+ at each frequency band and analysis window. Results for a broadband analysis (0.84–4.76 kHz) are shown in the bottom two rows for reference. Similar trends were seen for the results in the two analysis windows. Signal amplitude, SNR, MOC effects, and the number of participants included in the analysis tended to decrease with increasing frequency, consistent with our previous work (Mertes, 2018). Additionally, signal amplitude and SNR were higher in CAS− than in CAS+, consistent with a reduction due to activation of the MOC reflex. At a given frequency, the signal amplitude, SNR, and the number of participants included in the analysis tended to be larger for the TEOAE window than the SSOAE window. Median phase shifts were exhibited as phase leads and phase lags across frequencies, with no clear trend for TEOAEs or SSOAEs.

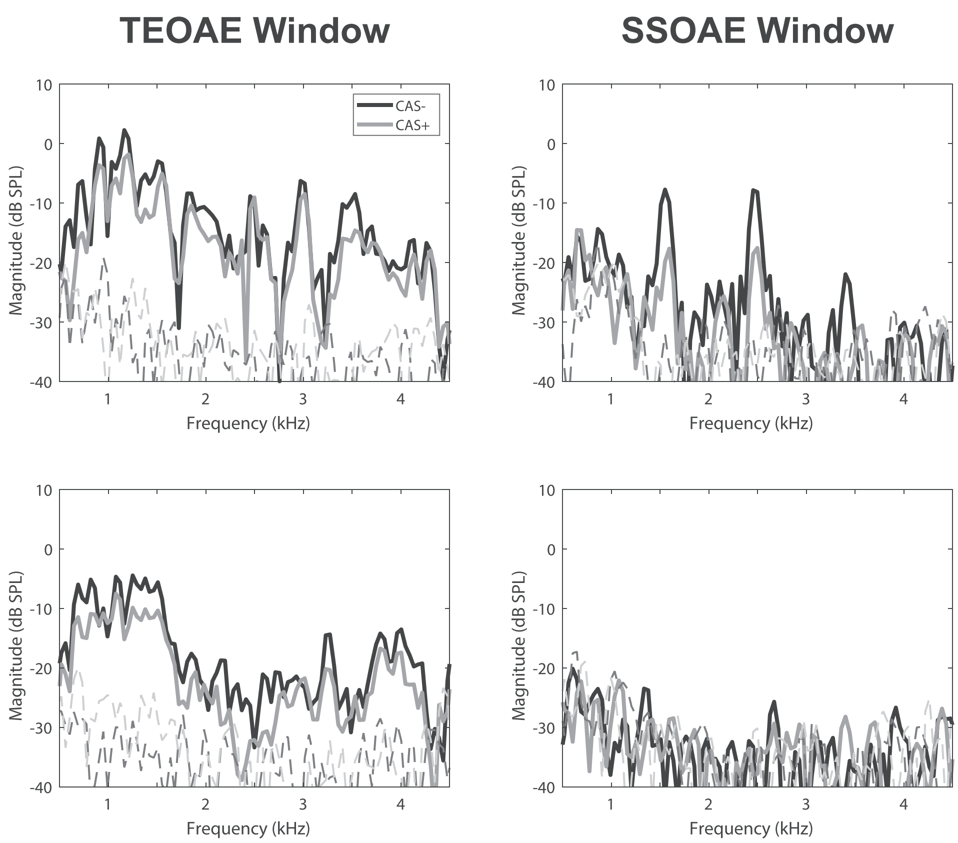

Fig. 1. Examples of otoacoustic emission spectra obtained in the TEOAE window (left column) and SSOAE window (right column). Black lines are used for results in CAS−. Gray lines are used for results in CAS+. Solid lines represent the signal magnitudes. Dashed lines represent the noise floor magnitudes. The top row shows results for one representative participant with prominent SSOAE peaks. The bottom row shows results for one representative participant without SSOAEs.

Table 1. Descriptive statistics for results at each analysis frequency and analysis window. Columns display the median followed by the interquartile range in parentheses, with the exception of the last column which shows the number and percentage of participants included in the analysis.

Center Frequency (kHz)	Window	CAS− Signal (dB SPL)	CAS− SNR (dB)	CAS+ Signal (dB SPL)	CAS+ SNR (dB)	MOC Effect (dB)	Phase Shift (cycles)	Number (Percent)
1	TEOAE	−2.67 (7.89)	25.11 (6.62)	−6.78 (7.27)	23.14 (8.96)	3.07 (2.09)	−0.08 (1.84)	26 (100%)
	SSOAE	−9.31 (11.32)	19.85 (11.21)	−16.93 (4.94)	14.07 (11.67)	9.24 (6.38)	−0.14 (1.00)	14 (53.85%)
1.4	TEOAE	−9.07 (7.61)	25.88 (9.78)	−11.71 (8.36)	19.83 (9.74)	2.79 (2.60)	0.02 (1.87)	26 (100%)
	SSOAE	−16.40 (8.62)	17.31 (7.97)	−21.34 (9.27)	11.47 (11.39)	6.28 (4.79)	0.05 (1.61)	16 (61.54%)
2	TEOAE	−18.43 (7.06)	17.55 (7.64)	−20.44 (6.27)	15.96 (6.99)	2.77 (2.82)	0.01 (1.88)	23 (88.46%)
	SSOAE	−19.69 (5.99)	18.04 (5.89)	−22.41 (7.66)	12.96 (8.67)	5.15 (8.05)	−0.40 (2.43)	10 (38.46%)
2.8	TEOAE	−20.10 (7.59)	17.08 (7.27)	−23.71 (6.93)	13.85 (6.17)	2.87 (1.60)	−0.09 (2.45)	22 (84.62%)
	SSOAE	−19.05 (3.48)	16.40 (4.93)	−22.31 (7.88)	14.30 (5.69)	2.50 (1.63)	−0.50 (2.28)	8 (30.77%)
4	TEOAE	−21.93 (10.62)	14.41 (7.23)	−24.41 (10.00)	11.98 (9.77)	2.08 (1.59)	0.02 (2.82)	14 (53.85%)
	SSOAE	−25.26 (9.99)	11.04 (7.65)	−27.26 (9.50)	9.36 (10.12)	2.00 (1.47)	−0.67 (4.23)	5 (19.23%)
Broadband	TEOAE	−18.82 (7.31)	16.98 (7.51)	−21.94 (7.31)	13.67 (7.39)	2.44 (1.35)	−0.21 (1.63)	24 (92.31%)
	SSOAE	−24.66 (5.23)	11.84 (3.62)	−27.98 (6.53)	6.74 (5.81)	3.42 (2.85)	−0.66 (0.81)	11 (42.31%)

Table 1 shows that median MOC effects were larger in the SSOAE window than in the TEOAE window from 1 to 2 kHz and for the broadband analysis. It is also of note that the spread of the data (IQR) was typically larger in the SSOAE window. Scatterplots of MOC effects in the TEOAE and SSOAE windows are shown in Fig. 2. From 1 to 2.8 kHz and for the broadband analysis, most data points were above the diagonal line, indicating larger MOC effects in the SSOAE window than in the TEOAE window. However, at a given frequency, the number of participants with present SSOAEs was lower than those with present TEOAEs. Therefore, the magnitude of MOC effects was compared between the two windows only for participants who had present TEOAEs and SSOAEs at a given frequency. Due to the small sample sizes, these comparisons were made using the nonparametric related-samples sign test (visual inspection revealed that the distribution of differences was not symmetric, so a Wilcoxon signed-rank test would not be appropriate). The median MOC effect was significantly larger in the SSOAE window than the TEOAE window for center frequencies of 1 kHz ($p = 0.013$) and 1.4 kHz ($p = 0.004$). There was no significant difference in median MOC effects between the two windows for center frequencies of 2 kHz ($p = 0.344$), 2.8 kHz ($p = 0.070$), 4 kHz ($p = 0.375$), and for the broadband analysis ($p = 0.065$). There were also no significant differences in median phase shifts between the two windows at any frequency ($p > 0.05$ in all cases).

Spearman rank correlation coefficients were computed to examine the associations in MOC effect magnitude between the two windows. There was a statistically significant correlation between MOC effects in the two windows for center frequencies of 1 kHz [$r_s(12) = 0.710$,

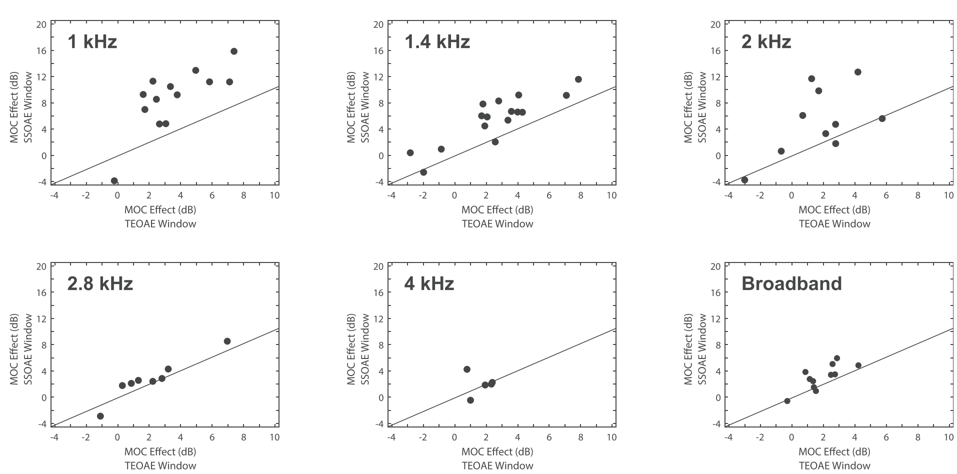

Fig. 2. Scatterplots of MOC effects in the SSOAE window against the MOC effects in the TEOAE window. The analysis center frequency is shown in the upper-left corner of each panel. The diagonal line represents a 1:1 correspondence in magnitude between the two windows.

$p = 0.004$], 1.4 kHz [$r_s(14) = 0.779$, $p = 0.0004$], 2.8 kHz [$r_s(6) = 0.976$, $p = 0.00003$], and for the broadband analysis [$r_s(9) = 0.664$, $p = 0.026$]. The correlations were not statistically significant for center frequencies of 2 kHz [$r_s(8) = 0.394$, $p = 0.260$] and 4 kHz [$r_s(3) = 0.000$, $p = 1.000$]. Correlations between phase shifts in the TEOAE and SSOAE windows were not significant at any frequency band ($p > 0.05$ in all cases).

4. Discussion

The prevalence of SSOAEs in our sample was in agreement with some work (Sisto *et al.*, 2001; Keefe, 2012) but lower than the 100% prevalence reported by others (Jedrzejczak *et al.*, 2008; Lewis, 2018), possibly due to methodologic differences. The finding of increased TEOAE SNR in participants who had measurable SSOAEs was consistent with findings of Lewis (2018) and Jedrzejczak *et al.* (2020). It is well-known that MOC reflex activation introduces magnitude decreases and phase leads for TEOAEs and for spontaneous OAEs obtained without external stimulation [e.g., Collet *et al.* (1990), Guinan *et al.* (2003), and Zhao and Dhar (2010)], consistent with an MOC-mediated decrease in outer hair cell amplification. Cases of phase lags in the presence of CAS have been reported [e.g., Mertes and Goodman (2016) and Goodman *et al.* (2018)], but the underlying mechanism for these phase lags is unclear. Additionally, it is unknown why SSOAEs would exhibit larger magnitude changes than TEOAEs, pointing to the need for further research to understand the mechanisms. The significant correlations between MOC reflex effects on TEOAEs and SSOAEs in the lower frequencies are consistent with the two OAE types sharing a common linear coherent reflection mechanism (Shera, 2003). The lack of significant correlations at 2 and 4 kHz may be due in part to a lack of statistical power from the small sample size and use of a nonparametric statistical test.

Normal-hearing individuals exhibit a considerable range of MOC effect magnitudes [e.g., Backus and Guinan (2007), Lewis (2018), and Mertes (2018)]. Maximizing the measurable MOC effect is important for making a determination of whether the MOC effect is present and for determining the relative strength of the effect (e.g., present but weak in comparison to a normative group). Our findings suggest that including the MOC effect on SSOAEs could improve the sensitivity for detecting and quantifying the MOC reflex, as posited by Lewis (2018). One way to examine the utility of the MOC effect on SSOAEs is to determine if including it with the MOC effect on TEOAEs improves the association between MOC reflex strength and performance on a perceptual task such as speech-in-noise testing compared to the MOC effect on TEOAEs alone.

We recommend that future investigations that use TEOAEs to study the MOC reflex also examine the presence of SSOAEs and the MOC effect on these SSOAEs to determine their potential utility, especially when examining associations with perceptual tasks, as well as to improve understanding of the mechanisms. The narrowband analysis appeared preferable to the broadband analysis because the narrowband analysis included more participants due to increased SNRs. Additionally, the MOC-mediated change in magnitude appeared to be a more useful metric than the change in phase, at least for the current dataset. A potential improvement to the methodology would be to increase the frequency resolution of the analysis (e.g., by increasing the sampling rate), which would allow for an analysis of the frequency shift in SSOAEs [as in Zhao and Dhar (2010) and other work]. The potential downside to the large MOC effects on SSOAEs is that it could interfere with assessments of the MEM reflex that utilize the ear-canal stimulus amplitude [see supplemental material of Mertes (2020)]. Although the large MOC reflex effects on SSOAEs did not appear to impact the results of the MEM reflex check in this study, we also recommend that future studies take into account the potential impact of SSOAEs on assessments of the MEM reflex that examine changes in the ear-canal stimulus.

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References and links

[1]MOC reflex effects in the interim time (18–34 ms) represent a transition between TEOAEs and SSOAEs (Keefe, 2012). A qualitative examination of the magnitude changes in this interim window showed larger changes than in the TEOAE window but smaller changes than in the SSOAE window (data not shown).

[2]A 9 dB SNR criterion is more stringent than the typical 6 dB criterion but less stringent than recommendations for detecting MOC reflex effects in individuals [e.g., Lewis (2018)]. Additionally, the analysis included data for participants whose SNRs were >9 dB in CAS− but <9 dB in CAS+ (12 cases for TEOAEs, 15 cases for SSOAEs, out of 130 total cases). Excluding these cases resulted in a non-significant correlation and sign test for magnitude changes at 1 kHz but did not affect the statistical outcomes at other frequencies.

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