RESEARCH ARTICLE

REVISED The effect of coffee on contralateral suppression of transient evoked otoacoustic emissions [version 2; peer review: 2 approved, 1 approved with reservations]

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Abstract

Background: Coffee is a popular non-alcoholic beverage consumed by humans across the world. It contains caffeine, which is a type of stimulant of the central nervous system. In the auditory system, it has a positive effect on auditory brainstem response and perception of speech in noise. Further, caffeine has an inhibitory effect in the cochlea, but studies have rarely investigated its effect on otoacoustic emissions (OAEs) in humans. OAEs are low-intensity sounds produced by the cochlea, which could be recorded in the ear canal. The present study was carried out to investigate the effect of coffee on transient evoked otoacoustic emission (TEOAE) and contralateral suppression of TEOAE.

Method: A total of 52 young adults participated in the study. A cross-over study design was used for the present investigation. The TEOAE and contralateral suppression of TEOAE were recorded before and after consumption of coffee and milk. The contralateral suppression of TEOAE was measured by presenting white noise to the contralateral ear at 40, 50, and 60 dB sound pressure level (SPL).

Results: The mean amplitude of TEOAE before and after consumption of coffee was similar in both ears. Further, the mean contralateral suppression of TEOAE was slightly larger after consumption of coffee in both ears. However, the mean difference was not significant in both the ears.

Conclusions: Based on the findings of present study, coffee has no significant effect on the amplitude of TEOAE and contralateral suppression of TEOAE.

Keywords

Otoacoustic emissions, TEOAE, Contralateral suppression, Coffee, Caffeine

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REVISED **Amendments from Version 1**

In the modified manuscript few changes have been made to figures, citations, and conclusions. Details about the amount of caffeine per cup of coffee and the acoustic reflex threshold for white noise is added to the manuscript. In addition, typological errors are corrected. In Figure 2 and Figure 3, Y-axis label has been modified. In Figure 4 error bars (standard deviation) are added. Few citations are added to the introduction section and errors in citations has been corrected.

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Introduction

Coffee is a non-alcoholic beverage which is widely consumed by humans across the world.[1–3] It contains a variety of bioactive chemicals that have anti-oxidant, anti-inflammatory, and anti-cancer properties.[1] It also contains caffeine which is a stimulating agent. Caffeine is also found in various other food items such as tea, cocoa beans, chocolate, energy drinks, among others.[1,2] The amount of caffeine in any food product is determined by the serving size, product type, and preparation method.[4] Caffeine improves perception, increases the ability to remain awake for longer periods, and reduces fatigue.[5] The stimulatory effect of caffeine is due to the blocking of adenosine receptors, consequently regulating the neurotransmitter levels and activities in the central nervous system.[3]

Otoacoustic emissions (OAEs) are very small amplitude sounds produced by the cochlea as a by-product of motile function of the outer hair cells (OHCs) (i.e. amplifier function of OHCs).[6,7] The OAEs generated in the cochlea travel backwards through the middle ear to the external ear canal, and it can be recorded using a sensitive microphone from the external ear canal.[6–8] In the cochlea, the OAEs are produced spontaneously and also in response to an external acoustic stimuli, referred as spontaneous OAEs and evoked OAEs respectively.[8] The OAEs are commonly elicited using clicks, tone-bursts, and pure-tones. The OAEs elicited using short-duration stimuli such as clicks and tone-bursts are known as transient evoked OAEs (TEOAEs).[6–8] The OAEs elicited using pure-tones are known as distortion product OAEs (DPOAEs) and stimulus frequency OAEs (SFOAEs).[8] The OAEs are very useful for assessing the cochlea and efferent pathways of the auditory system.

The human auditory system comprises afferent and efferent auditory pathways. The efferent pathways have an inhibitory function in the auditory system. In the cochlea, the efferent fibres cause hyperpolarization of OHCs, subsequently reducing their motile function.[9] The reduced motility of OHCs in the presence of efferent activity result in a reduction of the amplitude of OAEs.[10] This reduction in the amplitude of OAE due to efferent activity is called suppression of OAE. In humans, the suppression of OAE can be measured by presenting noise to the test ear or non-test ear during the recording of OAEs. The suppression of OAE obtained by presenting noise to the non-test ear is known as the contralateral suppression of OAE.[8]

Several studies have investigated the effect of caffeine on the auditory system. Studies have been carried out to investigate the effect of caffeine on auditory evoked potentials,[11–20] speech perception,[21,22] and OAEs.[23] Few studies have investigated the effect of caffeine on the auditory brainstem response (ABR). Findings from these investigations have showed significantly shorter latency and larger amplitude for ABR peaks following caffeine ingestion.[11,12,16] Similarly, the latency of peaks of the auditory middle latency response and the peak P1 of the auditory late latency response was decreased after caffeine ingestion.[12] In general, findings of the above studies suggest a positive effect (improved neural transmission) of caffeine on the central auditory pathway. Very few studies have investigated the effect of caffeine on speech perception ability.[21,22] Altin *et al.*[21] investigated the effect of caffeine on speech identification score in noise. Results showed a significant improvement for speech identification score in noise after caffeine ingestion. Taghavi *et al.*[22] investigated the short-term effect of caffeine on the acceptable noise level (ANL) in individuals with normal hearing. The results showed a significant reduction in the ANL after caffeine intake, suggesting that caffeine increases tolerance to noise, improving speech perception in noise. Based on findings from the above investigations, caffeine could be assumed to improve the perception of speech in noise.

Studies investigating the effect of caffeine on the OAEs in humans are scarce. Various studies investigating the effect of caffeine on the cochlea have reported that, the caffeine causes hyperpolarization of OHCs in the cochlea which suppress the amplifier function of OHCs.[24–26] Therefore, caffeine could be assumed to have a negative effect on the amplitude of OAEs. Recently, Drepath *et al.*[23] reported no significant effect of coffee on the amplitude of DPOAE. In contrast, Bobbin[27] reported a negative effect of caffeine on the amplitude of DPOAE in animal study. Therefore, although Drepath *et al.* [23] reported no effect of coffee on the amplitude of OAE in humans; similar investigations should be conducted before generalizing the results. Thus, the first objective of the present study was to investigate the effect of coffee on the amplitude of TEOAE. The second objective of the present study was to investigate the effect of coffee on the contralateral suppression of TEOAE, to understand the effect of caffeine on efferent activity in the auditory system. Studies investigating the effect of caffeine on the

ABR have reported an improved transmission of neural activity in the auditory pathway. This improved transmission in the afferent pathways could have an influence on the activity in the efferent pathways. However, none of the studies have investigated the effect of caffeine on the efferent auditory activity. Further, studies investigating the effect of caffeine on speech perception have reported a positive effect of caffeine on the perception of speech in noise. The improvement in speech perception after caffeine ingestion could be a consequence of increased efferent activity in the auditory system. In this connection, several studies have reported a significant relationship between the magnitude of efferent activity and speech perception in noise.[28,29] Therefore, there is a need to understand the effect of caffeine on the efferent activity.

Method

Participants

A total of 52 adults (nine males, 43 females) aged between 19 and 24 years (mean=21.65, standard deviation (SD)=1.36) participated in the study. All participants had hearing sensitivity within normal limits in both ears. The pure-tone threshold was less than 15 dB HL at octave frequencies from 250 Hz to 8000 Hz. Immittance evaluation showed 'A' type tympanogram with acoustic reflex present at normal levels in both ears. The acoustic reflex threshold for white noise was greater than 70 dB SPL for all the participants. None of the participants had a history of otological problems, such as ear pain, ear discharge etc. None of the participants reported exposure to loud sounds or ototoxic medication. Individuals who agreed to participate in the study were randomly assigned into two groups (coffee-first group and milk-first group) using drawing lots method. The study was approved by the institutional ethics committee of Kasturba Medical College, Mangalore (Protocol number: IEC KMC MLR 03-2021/89) and informed consent was obtained from all the participants.

Procedure

The data collection was carried out in two phases. In phase I, the TEOAE and contralateral suppression of TEOAE were recorded before and after consumption of coffee (coffee-first group) or milk (milk-first group). In phase II, the TEOAE and contralateral suppression of TEOAE were recorded before and after consumption of milk (coffee-first group) or coffee (milk-first group). Phase II of the study was carried out after a gap of one week. Further, participants were informed to restrain from consuming caffeinated substances such as coffee, tea, energy drinks, or chocolate. for at least 12 hours prior to data collection. The procedure followed for data collection is shown in Figure 1.

Recording of TEOAEs

The TEOAEs were recorded using the Otodynamics Echoport 292II otoacoustic emission analyzer. During the recording of TEOAEs, participants were made to sit comfortably on the reclining chair. They were instructed not to move throughout the duration of recording of TEOAEs. The OAE probe was inserted to the test ear and E-A-RTone 5A insert phone was inserted to the contralateral ear of participants. Initially, the TEOAE was recorded in non-linear mode. A total of 260 click-trains (1040 clicks) were presented at 80 dB SPL, and the responses were averaged. Following this, the TEOAEs were recorded in linear-mode. A total of four recordings were obtained with and without presenting noise to the contralateral ear of participants. In each recording, a total of 400 click-trains (1600 clicks) were presented at 60 dB SPL and the responses were averaged. The first recording of TEOAE was always obtained without presenting noise to the contralateral ear, and referred to as baseline TEOAE. The remaining three recordings were obtained by presenting white noise to the contralateral ear of participants at 60 dB SPL, 50 dB SPL, and 40 dB SPL. The order of noise level presented to the contralateral ear was randomized. All the recordings of TEOAE were obtained without disturbing the placement of OAE probe (*i.e.*, single-fit condition). Further, the TEOAEs were recorded from both ears of the participants.

The TEOAEs were recorded in four sessions. The first two sessions were scheduled on day 1 and the remaining two sessions were scheduled after one week. In the first session, the TEOAEs were recorded in non-linear and linear modes and these recordings were referred to as 'pre-drink measurements'. After completing the baseline measurements, coffee

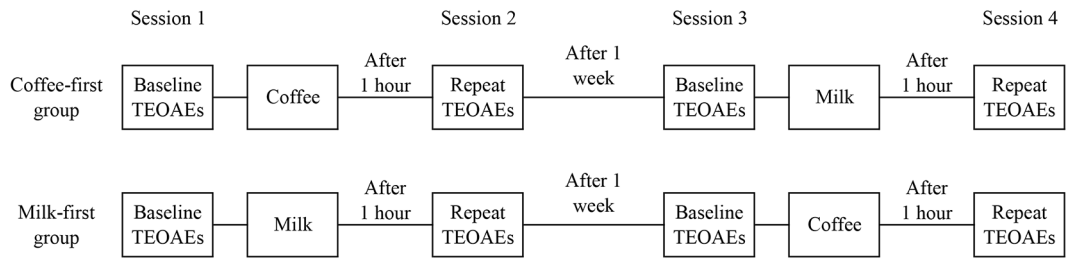

Figure 1. Schematic diagram showing the procedure followed for data collection. In each session TEOAEs were recorded in non-linear mode and in linear mode with and without delivering noise to the contralateral ear.

was given to participants in the 'coffee-first' group and milk was given to participants in the 'milk-first' group. After one hour, the second session of TEOAE recording was initiated. The procedure of recording TEOAEs in the second session was similar to the first session and referred as 'post-drink measurements'. After one week, the pre-drink (session 3) and post-drink (session 4) measurements were repeated. After the third session, milk was given to participants in the 'coffee-first' group and coffee was given to participants in the 'milk-first' group.

Coffee preparation

One sachet of instant coffee powder (1.3 g – 70% coffee and 30% chicory) and two tablespoons of powdered milk were mixed in 150 mL of warm water and sugar was added to improve the flavour for each serving. This is a method of coffee preparation followed in India. The amount of caffeine ranged from 27 to 40 mg per cup of coffee. Milk was prepared similarly without adding the coffee powder.

Data analysis

The global amplitude of TEOAE and noise-floor level was computed using EchoMaster software.[30] The TEOAEs recorded in non-linear and linear modes were considered present when the global signal-to-noise ratio (SNR) was at least 6 dB SNR. The magnitude of contralateral suppression of TEOAE was calculated by subtracting the global amplitude of TEOAE in various contralateral noise conditions (*i.e.*, 60, 50 and 40 dB SPL) from the baseline condition.

Results

Transient evoked otoacoustic emissions

Figure 2 shows the mean global amplitude of TEOAE (recorded in non-linear mode at 80 dB SPL) for both ears before and after consumption of coffee and milk. The mean amplitudes were similar for both ears across the conditions (*i.e.*, before and after consumption of coffee and milk). The Shapiro-Wilk test revealed that the amplitude of TEOAE of both ears across conditions was normally distributed. Thus, a repeated-measures ANOVA was carried out with ears (right and left), condition (before and after consumption), and drink (coffee and milk) as repeated measures. Results showed no significant effect of ear [F(1,42)=0.505, p=0.481], condition [F(1,42)=0.162, p=0.689], and drink [F(1,42)=0.644, p=0.427] on the amplitude of TEOAE. Further, no significant interaction was found between ears and condition [F(1,42)=2.016, p=0.163], drink and condition [F(1,42)=0.644, p=0.427], ears and drink [F(1,42)=0.09, p=0.765], and ears, drink, and conditions [F(1,42)=0.135, p=0.751]. Bayesian repeated measures-ANOVA showed moderate evidence in favour of the null hypothesis for the effect of condition [BF_{10}=0.127] and drink [BF_{10}=0.156] on the amplitude of TEOAEs. Further, it showed anecdotal evidence in favour of the null hypothesis for the effect of ears [BF_{10}=0.366] on the amplitude of TEOAE, which suggests more data/sample need to be collected to draw a firm conclusion.[31]

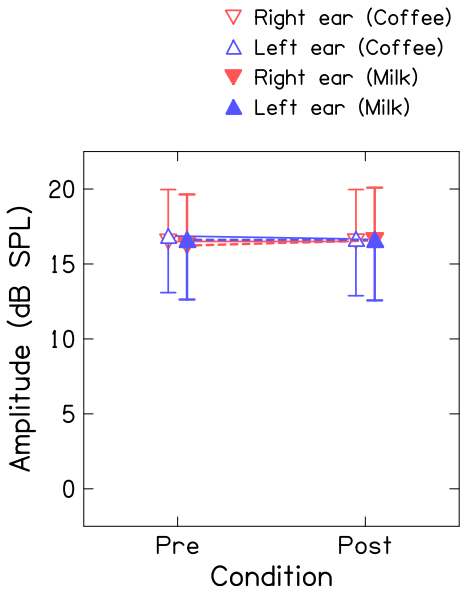

Figure 2. Mean global amplitude of TEOAE (recorded in non-linear mode at 80 dB SPL) before and after consumption of coffee (unfilled triangles connected with solid line) and milk (filled triangles with dashed line) for right ear (red colour) and left ear (blue colour).

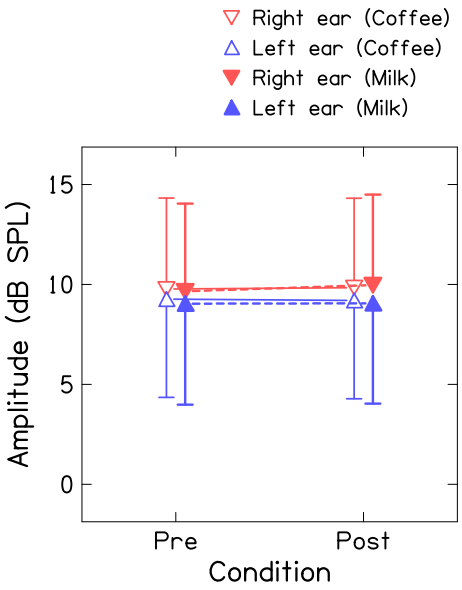

Figure 3. Mean global amplitude of TEOAE (recorded in linear mode at 60 dB SPL) before and after consumption of coffee (unfilled triangles connected with solid line) and milk (filled triangles with dashed line) for right ear (red colour) and left ear (blue colour).

Figure 3 shows the mean global amplitude of TEOAE (recorded in linear mode at 60 dB SPL) for both ears before and after consumption of coffee and milk. The mean amplitude of TEOAE was larger in the right ear across the conditions (*i.e.*, before and after consumption of coffee and milk). Further, the mean amplitudes of TEOAE before and after consumption of coffee or milk were similar for both ears. The Shapiro-Wilk test revealed that the amplitude of TEOAE of both ears across conditions was normally distributed. Repeated-measures ANOVA was carried out with ears (right and left), conditions (before and after consumption), and drink (coffee and milk) as repeated measures. Results showed no significant effect of ear [$F(1,46)=2.815$, $p=0.1$], condition [$F(1,46)=0.604$, $p=0.441$], and drink [$F(1,46)=0.288$, $p=0.594$] on the amplitude of TEOAE. Further, no significant interaction was found between ears and conditions [$F(1,46)=1.267$, $p=0.266$], drink and conditions [$F(1,46)=0.752$, $p=0.39$], ears and drink [$F(1,46)=0.959$, $p=0.333$], and ears, drink, and conditions [$F(1,46)=0.146$, $p=0.704$]. Bayesian repeated measures ANOVA showed extreme evidence in favour of the null hypothesis for the effect of conditions [$BF_{10}=0.002$] and drink [$BF_{10}= 0.002$] on the amplitude of TEOAEs. Further, it showed anecdotal evidence for the effect of ears [$BF_{10}=1$] on the amplitude of TEOAE which suggests more data need to be collected to draw a firm conclusion.[31]

Contralateral suppression of transient evoked otoacoustic emissions

Figures 4 and 5 show the mean magnitude of contralateral suppression of TEOAE for both ears across the levels of noise before and after consumption of coffee and milk. Panel A and panel B of Figure 4 show the mean contralateral suppression of TEOAE across noise levels for baseline measurement. The mean contralateral suppression was slightly lower in the left ear compared to the right ear. Further, the mean contralateral suppression of TEOAE decreased with the reduction in the level of noise in the contralateral ear. Panels C and D of Figure 4 show the mean contralateral suppression of TEOAE before and after consumption of coffee and milk respectively in the two ears. The results for the same are depicted in Figure 5 for better visualization. The mean contralateral suppression before and after consumption of milk was similar at each level of noise in the two ears. In contrast, a slightly greater suppression was noted after consumption of coffee at each level of noise in the two ears, except for the right ear at 40 dB noise.

The Shapiro-Wilk test revealed that the magnitude of contralateral suppression of TEOAE across conditions and levels of noise for both ears were not normally distributed. To investigate the effect of condition (before and after consumption) and drink (coffee and milk) on the contralateral suppression of TEOAE, the Friedman test was carried out separately for each ear (right and left). Results showed no significant difference for the magnitude of contralateral suppression of TEOAE before and after consumption of coffee and milk at each level of noise for right ear [60 dB ($\chi^2_{(3)}=4.021$, $p=0.259$) and left ear [60 dB ($\chi^2_{(3)}=3.952$, $p=0.267$)]. Further, to investigate the effect of ear on the contralateral suppression of TEOAE, the data obtained before consumption of coffee were subjected to the Wilcoxon signed ranks test. It showed the contralateral suppression of TEOAE was not significantly different between ears ($Z=1.208$, $p=0.227$).

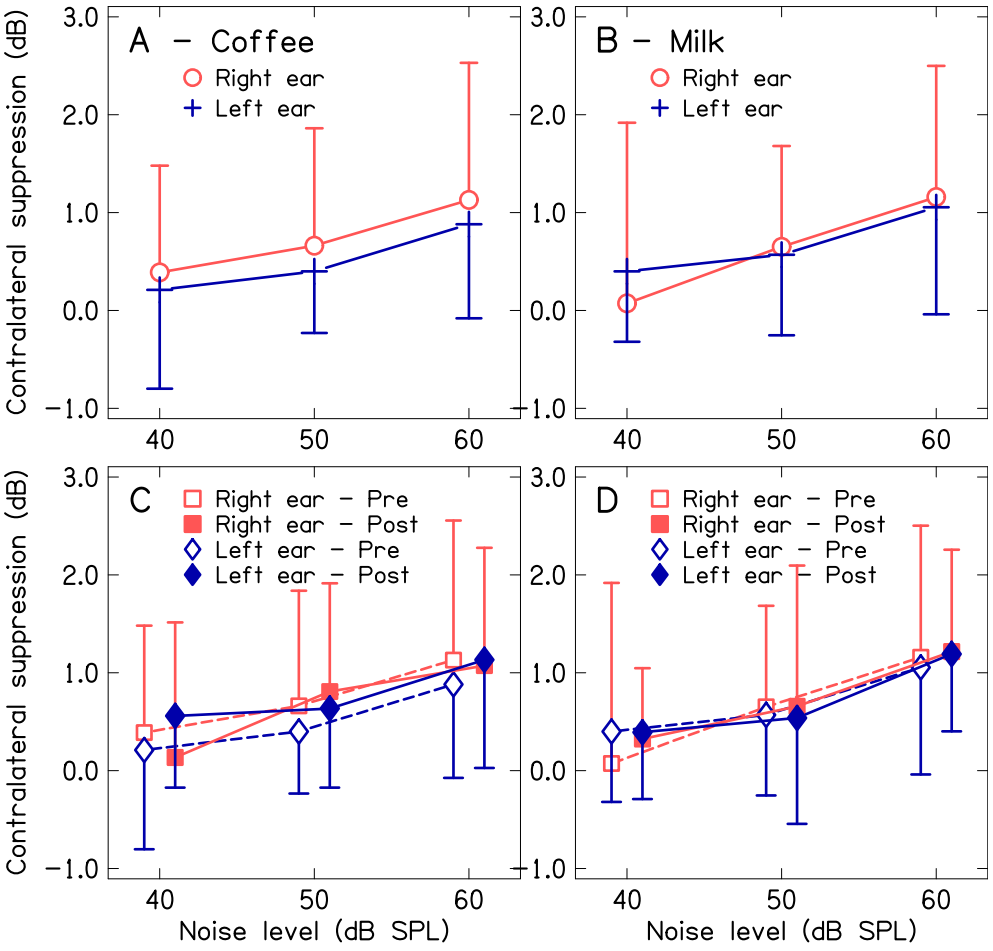

Figure 4. Mean magnitude of contralateral suppression of TEOAE before and after consumption of coffee and milk and across the levels on noise in the contralateral ear for both ears. Panel A shows the mean contralateral suppression of TEOAE for both ears before consumption of coffee. Panel B shows the mean contralateral suppression of TEOAE for both ears before consumption of milk. Panel C shows the mean contralateral suppression of TEOAE for both ears before and after consumption of coffee. Panel D shows the mean contralateral suppression of TEOAE for both ears before and after consumption of milk.

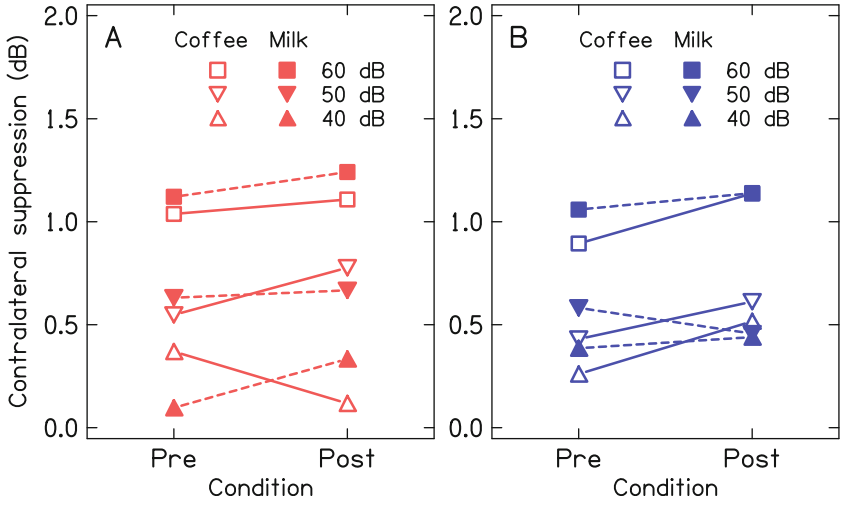

Figure 5. Mean magnitude of contralateral suppression of TEOAE across levels of noise in the contralateral ear before and after consumption of coffee and milk in right ear (panel A) and left ear (panel B).

Discussion

Results of the present study showed no significant effect of coffee on the amplitude of TEOAE. This finding is consistent with results of Drepath *et al.*[23] which showed no effect of coffee on the amplitude of DPOAEs in humans. These findings suggests no effect of caffeine on the amplitude of OAEs in humans. But, in contrast to the findings of human studies, animal studies have reported an effect of caffeine on the amplitude of DPOAEs. Bobbin[27] reported a stimulus level-dependent effect of caffeine on the amplitude of DPOAE. The amplitude of DPOAE was found to be reduced when elicited with lower-intensity stimuli and the amplitude was increased when elicited with higher-intensity stimuli. In addition, Bobbin[27] also investigated the effect of caffeine on the compound action potentials (CAP), summating potential (SP), cochlear microphonics (CM) and latency of N1. The caffeine had a suppressive effect on the CAP, SP, and latency of N1. Bobbin[27] attributed the reduction in the amplitude of DPOAE at low intensity to diminished amplifier function of OHCs in the cochlea, which is a consequence of caffeine. In the cochlea, caffeine causes activation of Ca^{2+}-dependent K^{+} channels in the OHCs, which leads to hyperpolarization of the OHCs and subsequently suppresses the amplifier function of OHCs.[24–26,32,33] Recently, Castellano-Muñoz *et al.*[34] investigated the effect of caffeine on the electrical properties of OHCs and postsynaptic activity in auditory fibers. The results showed caffeine has no effect on the electrical properties of OHCs, but it has an effect on the postsynaptic activity in auditory fibers. Thus, findings of the above study suggest that functioning of the OHCs may not be influences by caffeine, and hence the amplitude of OAE could be similar before and after consumption of caffeine.

The present study also investigated the effect of coffee on the contralateral suppression of TEOAE. The contralateral suppression of TEOAE was measured by presenting white noise to the contralateral ear at 40, 50, and 60 dB SPL. Results showed an increase in the magnitude of contralateral suppression of TEOAE with an increase in the level of noise in the contralateral ear. These findings are consistent with results of several investigations.[35–38] The increase in contralateral suppression of TEOAE with noise level has been attributed to the strength of efferent activity. Further, results of the present study showed a slightly greater contralateral suppression after coffee consumption; however, the difference was not significant. As studies investigating the effect of caffeine on the contralateral suppression of TEOAE are not available in the literature, the results of the present study cannot be compared with other investigations. Further, although findings of the present study showed no significant effect of coffee or caffeine on the contralateral suppression of TEOAE, similar studies are essential before generalizing the findings.

Based on the findings of the present study, we understand that consuming coffee before an audiological evaluation has no significant effect on the amplitude of TEOAE and contralateral suppression of TEOAE. However, there are few limitations to the present study. In the literature, studies investigating the effect of caffeine on the ABR have shown a dose-dependent effect of caffeine on the peaks of ABR.[16] A similar a dose dependent effect of caffeine could be present on the amplitude of TEOAE and contralateral suppression of TEOAE. However, in the present study a fixed amount of coffee was provided to participants, thus currently it is not understood whether increasing the dose of caffeine would have any effect on the amplitude of TEOAE and contralateral suppression of TEOAEs. Further, the amount of caffeine present in coffee is dependent on the type of coffee (*i.e.*, brewed, instant, or decaffeinated).[39,40] In the present study instant coffee was given to participants, which contains lower amount of caffeine compared to brewed coffee. Therefore, if coffee has a dose-dependent effects of caffeine on the TEOAE and contralateral suppression of TEOAE, then findings of the present study cannot be generalized to all types of coffee.

To conclude, findings of the present study suggest no effect of coffee on the findings of TEOAE. The procedure used for recording the non-linear TEOAE in the present research was similar to the protocol used in clinics for routine evaluation. Thus, based on findings of the present study, we understand that consuming coffee before an audiological evaluation may not affect clinical measurement of TEOAEs and the inferences drawn from it don't change with coffee consumption.

Data availability

Mendeley Data: The effect of coffee on TEOAE and contralateral suppression of TEOAE, https://doi.org/10.17632/p4pgd57zgd.1.[41]

This project contains the following underlying data:

- CSTEOAE_linear.csv (contains data of contralateral suppression of TEOAE)

- Read Me.txt (description to understand the variables in data files)

- TEOAE_linear.csv (contains data of amplitude of TEOAE recorded in linear mode in baseline and contralateral conditions)

- TEOAE_non-linear.csv (contains data of amplitude of TEOAE recorded in non-linear mode)

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Publisher Full Text

Open Peer Review

Current Peer Review Status: ? ✓ ✓

Version 2

Reviewer Report 09 November 2023

https://doi.org/10.5256/f1000research.155503.r206293

?

Wiktor Jedrzejczak
World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland

I appreciate all the corrections. I have some further suggestions for improvement of the manuscript.

There is very limited number of references to OAE studies. All cited OAE studies except one are older than 20 years. There is a plenty of recent studies to which the authors could refer to. On the other hand when introducing OAEs I suggest to reference at least one paper by David Kemp who discovered them.

When citing a book (reference number 8) please cite actual pages to which you refer or alternatively please cite the papers which are related to this area.
Please try to more clearly formulate the aim of the study. The sentence “Therefore, there is a need to understand the effect of caffeine on the efferent activity.” Is rather vague.

Indeed, there are no studies on suppression of OAE in relation to coffee, but there are studies showing what are the fluctuations of suppression or what are the differences in suppression across measurements at the same day. There are even studies done on the same type of equipment. Please try to compare present results to these studies.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Neuroscience, audiology, signal processing, otoacoustic emissions

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 11 October 2023

https://doi.org/10.5256/f1000research.155503.r206294

Sandeep Maruthy
Department of Audiology, All India Institute of Speech and Hearing, Mysuru, Karnataka, India

I can find that the revised manuscript is in a much better shape with authors addressing all the concerns raised. The manuscript can be accepted for indexing, provided the authors address some minor concerns listed below:

1) In the page 8, the authors state, 'As studies investigating the effect of caffeine on the contralateral suppression of TEOAE are not available in the literature', which is not true. They themselves have quoted Drepath et al. at many instances in the article. I suggest rephrasing.

2) The authors in the Introduction section claim that their study will help in generalizing the results of Drepath et al., who did not find significant difference of coffee consumption on CSOAEs. The authors in this study found results similar to Drepath et al. Yet, they conclude that 'similar studies are essential before generalizing the results' (same statement repeated). This surprises me. When two studies at different points of time, by different groups of researchers have shown the same results, what is the reason for authors to call for another such study? How is that expected to be different? In my opinion it is not required. I suggest that authors discuss it differently.

3) The findings support the absence of effect for dosage used in this study (1.3g coffee powder mixed with two spoons of powdered milk & 150 mL water). During the discussion of their results, the authors, rightly so, speculate dose dependent effect of caffeine. I suggest the authors to state clearly that dosage of caffeine used in this study or any lower than this will not lead to significant effects on CSOAEs. However, the effect of caffeine dosage higher than that used in the study needs to be explored in future.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Audiology, electrophysiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 06 October 2023

https://doi.org/10.5256/f1000research.155503.r206292

Chhayakant Patro
Department of Speech-Language Pathology & Audiology, Towson University, Towson, MD, USA

I am delighted to accept this paper for publication as the authors have comprehensively addressed all the concerns raised during the last peer review process.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Peripheral physiology, speech perception, and aging

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 13 December 2022

https://doi.org/10.5256/f1000research.134894.r146365

?

Sandeep Maruthy
Department of Audiology, All India Institute of Speech and Hearing, Mysuru, Karnataka, India

The study compared the amplitude of OAEs and the magnitude of contralateral suppression of OAEs before and after consuming coffee. The results show no significant difference between the two conditions, which the authors interpret as '*no effect of coffee on OAEs and contralateral suppression of OAEs.*' The authors have used a robust research design, an acceptable sample size and have made reasonable attempts to control the possible extraneous variables. Overall, I appreciate the authors for their work. It is a work worth indexing and of interest to the potential readers of this journal. However, the manuscript needs a significant revision before I can recommend this for indexing. Following are my section-wise comments (a few of them in the form of questions to the authors) which I suggest the authors consider while revising the manuscript.

Title
The title reflects only the contralateral suppression of TEOAEs, and misses out on reflecting the amplitude of OAEs.

Abstract
The background should highlight the need for the study. Just stating that studies have rarely investigated its effect on OAEs may not be sufficient to justify the need for the current study.
I suggest the authors to confine the reporting to the statistical test findings and not report the mean difference in the abstract.
The abstract may have to be re-written after considering the comments of the other sections.

Introduction

- The authors must explain in more detail the influence of caffeine on the biochemistry due to which they expect OAEs and contralateral suppression of OAEs (CSOAEs) to change. The last sentence of the first paragraph mentions it in brief. The authors can elaborate it in the context of OAEs and CSOAEs. Also, later in the Discussion section, the authors have explained it based on Castellano-Muñoz et al. and Bobbin's studies, which needs mention in introduction.

- The word '*Further*' is not necessary in a couple of instances in the first two paragraphs and I suggest removing it.

- The transition of thought from the second to the third paragraph could be smoother. I suggest the authors make the necessary change.

- The abbreviation 'OAEs' once used, needs to be continued. For example, second line of the fourth paragraph has the full form.

- In the second line of the fifth paragraph, the sentence should read as '*caffeine on the cochlea have reported that*' instead of '*caffeine on the cochlea have reported.*'

- What is a positive effect? Needs clarity.

- Earlier studies have shown improvement in SPIN with caffeine intake; changes in SPIN are associated with changes in CSOAES; therefore, the authors expected caffeine intake to change the CSOAEs. However, the justification is not clearly narrated in the manuscript.

- Drepath et al. reported no significant effect of coffee on the amplitude of DPOAEs, but Bobbin found a significant effect. The presence of equivocal findings among previous studies alone cannot justify taking up a new study. I suggest that the authors critically analyze the method used in these studies and identify the reason for differences in the findings, to justify the study and the to support the method used here.

- The earlier studies have used DPOAEs while in the current study the authors used TEOAEs. Why did the authors prefer TEOAEs over DPOAEs? Considering that the physiological mechanisms of these two types of OAEs are different, can we not expect different findings in the two? If so, is it reasonable to compare the current findings with that of the previous studies where a different type of OAE was used?

- The statement '*This improved transmission in the afferent pathways could also elicit stronger activity in the efferent pathway*' needs to be supported with a citation.

- In the statement '*However, none of the studies have investigated the effect of caffeine of the efferent activity*', I think the authors are referring to 'efferent auditory activity'. Please specify.

- Many studies have shown an association between CSOAEs and SPIN. All of them need to be cited in the manuscript. For example, Maruthy et al. (2017). Also, not all the studies that probed this relationship have shown association between the two. Therefore, I prefer that

the authors mention '*some of the studies that probed ……*'

Method

- How was the sample size determined? Give details.
- The statement '*The acoustic reflex threshold for white noise was greater than 70 dB SPL for all the participants*' can be moved to earlier in the paragraph
- The first sentence in the procedure is a repetition of what is in the previous paragraph. Remove it from the procedure.
- '*Fitted to the ear test ear*' and '*fitted to the contralateral ear*' can be changed to 'inserted'
- What was the need to record contralateral suppression at 3 different noise levels? Did the authors expect differential effects of coffee across suppressor intensities? This needs a strong justification in the manuscript. Otherwise, I suggest that the authors present results of either 50dBSPL or 60dBSPL alone. If they wish to retain it as it is, intensity as a variable needs a mention and justification in the Introduction section.
- I have a similar comment for recording the effect in both ears of the subjects. Did the authors expect different effects in the two ears? If so, it needs to be justified.
- I suggest that the authors explain the significance of recording OAEs in both linear and nonlinear paradigms. Considering that contralateral suppression of OAEs is higher in the linear paradigm, the authors could have restricted it to only the linear paradigm.
- It is stated that '*All the recordings of TEOAE were obtained without disturbing the placement of OAE probe (i.e., single-fit condition)*'. The authors need to specify what measures they took to ensure that probe did not move while drinking coffee or milk, and in the next 1 hour until the second recording of OAEs was made.
- As I understood, the authors recorded CSOAEs after the baseline TEOAEs. I do not see a mention of that either in the text or in the Figure 1. Please make the necessary change.
- Mention the rationale for 1-hour interval after coffee consumption.
- The statement '*The TEOAEs obtained in the second session were similar to the first session and were referred as 'follow-up measurements*'. Do authors mean that the procedure was the same?
- Rather than calling them '*baseline*' and '*follow up*' measurements, I suggest 'pre-drink' and 'post-drink' measurements. This I think these terms will also compliment with the term given for this variable (drink) in the results section.
- Coffee preparation is one of the methods used in India. For example, coffee in USA is typically not prepared with milk or milk powder. I suggest the authors to mention that this is a method of coffee preparation followed in India.
- Please explain the rationale for using 1.3g of coffee. How does it relate to the coffee dosage

used in the earlier studies?

- As mentioned earlier, Figure 1 does not reflect CSOAE measurements.
- Provide supporting reference to the 6 dB and 3dB criteria used.
- The presence of 6dB in nonlinear mode and 3 dB in linear mode should have been a participant selection criterion.
- I suggest that the authors mention the target response measures in the method section.

Results

- The authors should talk about the normality test upfront and then describe the trend in the mean amplitude.
- '*conditions*' to be changed to 'condition'
- In Figure 2, I believe the unit is dB SPL. Please specify.
- Comparing between ears and across intensities of suppressors needs to be stated in the objectives. Otherwise, I suggest the authors to remove it from the results section.
- In the results of CSOAEs, the normality test revealed non-normal distribution of the data. Accordingly, Friedman test is used. In such a case, presenting median and IQR is more meaningful than mean and SD.
- '*both ears*' to be changed to 'in the two ears' in several places.
- Error bars or the appropriate measure of variance is not reflected in Figure 4 and 5. Please include. I suggest to show median and IQR.
- The Y-axis in Figure 4 and 5 should read as 'magnitude of CSOAEs (dB)'.
- The information in Figures 4 and 5 are the same but represented differently. I suggest retaining Figure 5 and removing Figure 4.

Discussion

- The statement '*The findings of the above study suggest that functioning of the OHCs may not be affected by caffeine, and thus the amplitude of OAE could be similar before and after consumption of caffeine*' is too profound for what authors can derive from their study. It should be read in the context of the dosage of coffee used in this study. I suggest that the authors tone down the inference drawn.
- This study showed the absence of significant effect of coffee on CSOAEs in presence of improvement in SPIN (as shown by earlier studies). Does it reflect that improvements in SPIN observed by them is not efferent mediated? The authors can consider discussing this direction.
- The results showed some effect, but that was not significant. Therefore, instead of concluding it as '*findings of the present study showed no effect of coffee on the findings of*

TEOAE' the authors can phrase it as 'findings suggest no effect of coffee'.

- The authors in the last statement of the manuscript state '*may not have negative effects on the amplitude of TEOAE,*' but earlier in the manuscript, they expected positive effects. This is contradictory. I believe they meant that clinical measurement of TEOAEs and the inferences drawn from it don't change with coffee consumption. Please make changes in the statement accordingly.

- To summarize, one may find more criticisms in my peer-review report than appreciations. This does not take away the credit for the good work done by the authors and the significant contribution of their work to science. I suggest that they revise it based on the inputs provided and submit the revised manuscript for reconsideration.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Audiology, electrophysiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 01 Sep 2023

Mohan Kalaiah

We thank you for peer reviewing the manuscript.

Based on your recommendations, manuscript has been modified. See details below:

Title
Reviewer comment: The title reflects only the contralateral suppression of TEOAEs, and misses out on reflecting the amplitude of OAEs.
Authors reply: Title changed to "The effect of coffee on transient evoked otoacoustic emissions and contralateral suppression of transient evoked otoacoustic emissions"

Abstract
Reviewer comment: The background should highlight the need for the study. Just stating that studies have rarely investigated its effect on OAEs may not be sufficient to justify the need for the current study.
I suggest the authors to confine the reporting to the statistical test findings and not report the mean difference in the abstract.
The abstract may have to be re-written after considering the comments of the other sections.
Authors reply: Statement on mean difference was removed from the abstract. Abstract modified

Introduction
Reviewer comment: The authors must explain in more detail the influence of caffeine on the biochemistry due to which they expect OAEs and contralateral suppression of OAEs (CSOAEs) to change. The last sentence of the first paragraph mentions it in brief. The authors can elaborate it in the context of OAEs and CSOAEs. Also, later in the Discussion section, the authors have explained it based on Castellano-Muñoz et al. and Bobbin's studies, which needs mention in introduction.
Authors reply: We agree with the recommendation

Reviewer comment: The word '*Further*' is not necessary in a couple of instances in the first two paragraphs and I suggest removing it.
Authors reply: removed

Reviewer comment: The transition of thought from the second to the third paragraph could be smoother. I suggest the authors make the necessary change.
Authors reply: modified

Reviewer comment: The abbreviation 'OAEs' once used, needs to be continued. For example, second line of the fourth paragraph has the full form.
Authors reply: modified

Reviewer comment: In the second line of the fifth paragraph, the sentence should read as '*caffeine on the cochlea have reported that*' instead of '*caffeine on the cochlea have reported.*'
Authors reply: modified

Reviewer comment: What is a positive effect? Needs clarity.
Authors reply: Positive effect refer to improved neural transmission. Same has been added to the manuscript.

Reviewer comment: The earlier studies have used DPOAEs while in the current study the

authors used TEOAEs. Why did the authors prefer TEOAEs over DPOAEs? Considering that the physiological mechanisms of these two types of OAEs are different, can we not expect different findings in the two? If so, is it reasonable to compare the current findings with that of the previous studies where a different type of OAE was used?
Authors reply: Yes, we agree that different findings are possible. TEOAEs were used in the present study as studies measuring the TEOAEs are not available in literature.

Reviewer comment: The statement '*This improved transmission in the afferent pathways could also elicit stronger activity in the efferent pathway*' needs to be supported with a citation.
Authors reply: Statement modified to '*This improved transmission in the afferent pathways could have an influence on the activity in the efferent pathway*'

Reviewer comment: In the statement '*However, none of the studies have investigated the effect of caffeine of the efferent activity*', I think the authors are referring to 'efferent auditory activity'. Please specify.
Authors reply: modified. 'efferent activity' changed to 'efferent auditory activity'

Reviewer comment: Many studies have shown an association between CSOAEs and SPIN. All of them need to be cited in the manuscript. For example, Maruthy et al. (2017). Also, not all the studies that probed this relationship have shown association between the two. Therefore, I prefer that the authors mention '*some of the studies that probed .....*'
Authors reply: references added.

Method

Reviewer comment: The statement '*The acoustic reflex threshold for white noise was greater than 70 dB SPL for all the participants*' can be moved to earlier in the paragraph
Authors reply: done

Reviewer comment: The first sentence in the procedure is a repetition of what is in the previous paragraph. Remove it from the procedure.
Authors reply: removed

Reviewer comment: '*Fitted to the ear test ear*' and '*fitted to the contralateral ear*' can be changed to 'inserted'
Authors reply: done

Reviewer comment: What was the need to record contralateral suppression at 3 different noise levels? Did the authors expect differential effects of coffee across suppressor intensities? This needs a strong justification in the manuscript. Otherwise, I suggest that the authors present results of either 50dBSPL or 60dBSPL alone. If they wish to retain it as it is, intensity as a variable needs a mention and justification in the Introduction section.
Authors reply: As the paper is already published we decided not to remove the data from the manuscript. However, for the purpose of statistical analysis only 60 dB noise was considered.
Reviewer comment: I have a similar comment for recording the effect in both ears of the subjects. Did the authors expect different effects in the two ears? If so, it needs to be

justified.
Authors reply: Many studies have documented a higher contralateral suppression of OAE in the right, suggesting an asymmetry in the magnitude of suppression between ears. Thus, in the present investigation the effect of caffeine on the contralateral suppression of TEOAE was measured in both ears.

Reviewer comment: I suggest that the authors explain the significance of recording OAEs in both linear and nonlinear paradigms. Considering that contralateral suppression of OAEs is higher in the linear paradigm, the authors could have restricted it to only the linear paradigm.
Authors reply: Non-linear TEOAEs are commonly recorded for clinical applications. While linear TEOAEs are commonly used during measurement of contralateral suppression of TEOAE. As recommended, in the present study, the contralateral suppression of TEOAE was measured using linear TEOAE only.

Reviewer comment: It is stated that '*All the recordings of TEOAE were obtained without disturbing the placement of OAE probe (i.e., single-fit condition)*'. The authors need to specify what measures they took to ensure that probe did not move while drinking coffee or milk, and in the next 1 hour until the second recording of OAEs was made.
Authors reply: All the recordings in one session was obtained in single-fit condition. Two sessions were present in one day with a gap of 1 hour (before and after).

Reviewer comment: As I understood, the authors recorded CSOAEs after the baseline TEOAEs. I do not see a mention of that either in the text or in the Figure 1. Please make the necessary change.
Authors reply: Yes, initially 'baseline' TEOAE was recorded and after that the TEOAE was recorded by delivering noise to the contralateral ear.

Reviewer comment: Mention the rationale for 1-hour interval after coffee consumption.
Authors reply: The effects from caffeine reach peak levels after 30 to 45 minutes of consumption. Thus, 1-hour interval was used between sessions.

Reviewer comment: The statement '*The TEOAEs obtained in the second session were similar to the first session and were referred as 'follow-up measurements*'. Do authors mean that the procedure was the same?
Authors reply: Yes

Reviewer comment: Rather than calling them '*baseline*' and '*follow up*' measurements, I suggest 'pre-drink' and 'post-drink' measurements. This I think these terms will also compliment with the term given for this variable (drink) in the results section.
Authors reply: done

Reviewer comment: Coffee preparation is one of the methods used in India. For example, coffee in USA is typically not prepared with milk or milk powder. I suggest the authors to mention that this is a method of coffee preparation followed in India.
Authors reply: Agreed and added to manuscript

Reviewer comment: Please explain the rationale for using 1.3g of coffee. How does it relate to the coffee dosage used in the earlier studies?
Authors reply: 1.3 g was the amount of coffee available in one sachet. It is typical serving size for one cup of coffee.

Reviewer comment: As mentioned earlier, Figure 1 does not reflect CSOAE measurements.
Authors reply: Details added to the legend of figure.

Reviewer comment: The presence of 6dB in nonlinear mode and 3 dB in linear mode should have been a participant selection criterion.
Authors reply: Agreed. We used 6 dB SNR in nonlinear mode as one of the criterion for participant selection in the present study. In linear mode, when the SNR was less than 6 dB OAE was considered as absent.

Reviewer comment: I suggest that the authors mention the target response measures in the method section.
Authors reply: We measured amplitude of TEOAE in non-linear and linear modes and magnitude of contralateral suppression of TEOAE. Same is mentioned in data analysis section.

Results
Reviewer comment: The authors should talk about the normality test upfront and then describe the trend in the mean amplitude.
Authors reply: Results of normality tests are provided in the manuscript.

Reviewer comment: '*conditions*' to be changed to 'condition'
Authors reply: done

Reviewer comment: In Figure 2, I believe the unit is dB SPL. Please specify.
Authors reply: SPL added

Reviewer comment: Comparing between ears and across intensities of suppressors needs to be stated in the objectives. Otherwise, I suggest the authors to remove it from the results section.
Authors reply: We prefer not to add the comparison across level of noise as an objective.

Reviewer comment: '*both ears*' to be changed to 'in the two ears' in several places.
Authors reply: done

Reviewer comment: The Y-axis in Figure 4 and 5 should read as 'magnitude of CSOAEs (dB)'.
Authors reply: Axis changed

Reviewer comment: The information in Figures 4 and 5 are the same but represented differently. I suggest retaining Figure 5 and removing Figure 4.
Authors reply: As manuscript is already published we prefer to retain both the figures.

Discussion
Reviewer comment: The statement '*The findings of the above study suggest that functioning of the OHCs may not be affected by caffeine, and thus the amplitude of OAE could be similar before and after consumption of caffeine'* is too profound for what authors can derive from their study. It should be read in the context of the dosage of coffee used in this study. I suggest that the authors tone down the inference drawn.
Authors reply: Modified

Reviewer comment: This study showed the absence of significant effect of coffee on CSOAEs in presence of improvement in SPIN (as shown by earlier studies). Does it reflect that improvements in SPIN observed by them is not efferent mediated? The authors can consider discussing this direction.
Authors reply: Could be mediated by efferent activity. Findings of Castellano-Muñoz *et al.* has revealed that caffeine resulted in changes in post-synaptic activity in auditory fibers in the absence of changes in OHCs. Thus, involvement of efferent activity may not be ruled out.

Reviewer comment: The results showed some effect, but that was not significant. Therefore, instead of concluding it as '*findings of the present study showed no effect of coffee on the findings of TEOAE' the authors can phrase it as 'findings suggest no effect of coffee*'.
Author reply: modified

Reviewer comment: The authors in the last statement of the manuscript state '*may not have negative effects on the amplitude of TEOAE,*' but earlier in the manuscript, they expected positive effects. This is contradictory. I believe they meant that clinical measurement of TEOAEs and the inferences drawn from it don't change with coffee consumption. Please make changes in the statement accordingly.
Author reply: Agreed

Reviewer comment: To summarize, one may find more criticisms in my peer-review report than appreciations. This does not take away the credit for the good work done by the authors and the significant contribution of their work to science. I suggest that they revise it based on the inputs provided and submit the revised manuscript for reconsideration.
Author reply: Thank you for agreeing to review the manuscript and providing recommendations.

Competing Interests: No competing interests were disclosed.

Reviewer Report 01 December 2022

https://doi.org/10.5256/f1000research.134894.r153018

Chhayakant Patro
Department of Speech-Language Pathology & Audiology, Towson University, Towson, MD, USA

This manuscript reports the results of an experiment that investigated the effects of caffeine intake on transient evoked otoacoustic emissions (TEOAEs) and contralateral suppression of TEOAEs, in a group of young listeners with normal hearing (N = 52). The results indicated that caffeine intake had no effects on absolute TEOAE amplitudes and had negligible effects on the contralateral suppression of TEOAEs. The following sections of general comments summarize my main comments and concerns. Specific comments (e.g., line-by-line editing) are not included as the line numbers are not available (to me).

- The use of cross-over design is innovative. Some individuals may have a greater sensitivity to the effects of caffeine than others and by treating each participant as his/her own control, such individual differences were accounted for.

- Any general comments regarding the effects of caffeine on auditory/ speech perception could be removed from the introduction section since the experiment focused on physiological effects and not on the perceptual consequences of caffeine consumption.

- Some sections of the manuscript are questionable because of a lack of coherence, and under-developed arguments. For example, the authors should give a clearer motivation for the choice of stimuli and conditions. Why did the authors hypothesize that TEOAEs could be more sensitive to the effects of caffeine than the DPOAEs (since the DPOAEs have produced null results, as the authors rightly acknowledge)?

- Throughout the paper (including the discussion section), comparisons to DPOAEs should be limited.

- "*Further, studies investigating the effect of caffeine on the speech perception have reported a positive effect of caffeine on the perception of speech in noise.*" – citations are needed here. Were the "positive effects" mediated by improved efferent activity? If not, those results are not relevant here.

- Although the authors cite some of the classic studies on OAEs, more recent citations are needed.

- Precisely how much caffeine was provided to the study participants?

- Were the acoustic reflexes present at all the test frequencies?

- Did the authors conduct an interview/ provide a questionnaire to determine whether the participants had a history of otological problems? Did the authors quantify the amount of noise exposure? This information is relevant because prolonged/repetitive exposure to loud sounds may lead to (subclinical) cochlear dysfunction and may obscure the observation of any potential relationship between caffeine consumption and cochlear function. At least, this needs to be addressed in the discussion section.

- Involving a large group of participants is a major strength.

- "*Further, the TEOAEs recorded in the linear mode were considered to be present if the global SNR was at least 3 dB SNR*." Citation(s) needed here. Was the +3 dB SNR criterion based on previous studies?
- Dienes, 2014: numeric reference formatting need.
- The statistical analyses did not reveal significant effects of caffeine consumption on contralateral suppression of TEOAEs. Still, the authors claim that "*TEOAE was slightly larger after consumption of coffee in both ears*" in the abstract, based on their qualitative judgment. Their observations may be highlighted in the discussion section, not in the abstract.
- What do the error bars in figures 2 and 3 depict?
- Please provide error bars in figures 4 and 5.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Peripheral physiology, speech perception, and aging

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 01 Sep 2023

Mohan Kalaiah

We thank you for peer reviewing the manuscript.

Based on your recommendation manuscript has been modified. See details below:

Reviewer comment: Any general comments regarding the effects of caffeine on auditory/ speech perception could be removed from the introduction section since the experiment focused on physiological effects and not on the perceptual consequences of caffeine consumption.
Authors reply: Agree. But no changes made to the manuscript.

Reviewer comment: Some sections of the manuscript are questionable because of a lack of coherence, and under-developed arguments. For example, the authors should give a clearer motivation for the choice of stimuli and conditions. Why did the authors hypothesize that TEOAEs could be more sensitive to the effects of caffeine than the DPOAEs (since the DPOAEs have produced null results, as the authors rightly acknowledge)?
Authors reply: Agree. We aimed to investigate the effect of coffee on the TEOAE.

Reviewer comment: Throughout the paper (including the discussion section), comparisons to DPOAEs should be limited.
Authors reply: DPOAE results are included as TEOAE results are not available in literature.

Reviewer comment: "*Further, studies investigating the effect of caffeine on the speech perception have reported a positive effect of caffeine on the perception of speech in noise.*" – citations are needed here. Were the "positive effects" mediated by improved efferent activity? If not, those results are not relevant here.
Authors reply: Studies have been cited. We do not know if positive effects are mediated by efferent activity.

Reviewer comment: Although the authors cite some of the classic studies on OAEs, more recent citations are needed.
Authors reply: References added

Reviewer comment: Precisely how much caffeine was provided to the study participants?
Authors reply: The amount of caffeine ranged from 27 to 40 mg per cup of coffee. Same information is added to the manuscript.

Reviewer comment: Were the acoustic reflexes present at all the test frequencies?
Authors reply: The acoustic reflex threshold was measured for puretones of frequency 500 Hz, 1000 Hz, 2000 Hz, and 4000 Hz and white noise.

Reviewer comment: Did the authors conduct an interview/ provide a questionnaire to determine whether the participants had a history of otological problems? Did the authors quantify the amount of noise exposure? This information is relevant because prolonged/repetitive exposure to loud sounds may lead to (subclinical) cochlear dysfunction and may obscure the observation of any potential relationship between caffeine consumption and cochlear function. At least, this needs to be addressed in the discussion section.
Authors reply: Yes, details were conducted through interview.

Reviewer comment: Involving a large group of participants is a major strength.

Reviewer comment: "*Further, the TEOAEs recorded in the linear mode were considered to be present if the global SNR was at least 3 dB SNR*." Citation(s) needed here. Was the +3 dB SNR criterion based on previous studies?
Authors reply: Earlier studies measuring contralateral suppression of OAE have used 3 dB SNR criterion. But, recent literature recommends 6 dB SNR or higher SNR for greater reliability. The data was reanalyzed with 6 dB SNR criterion and results are reported.

Reviewer comment: Dienes, 2014: numeric reference formatting need.
Authors reply: done

Reviewer comment: The statistical analyses did not reveal significant effects of caffeine consumption on contralateral suppression of TEOAEs. Still, the authors claim that "*TEOAE was slightly larger after consumption of coffee in both ears*" in the abstract, based on their qualitative judgment. Their observations may be highlighted in the discussion section, not in the abstract.
Authors reply: Abstract modified

Reviewer comment: What do the error bars in figures 2 and 3 depict?
Authors reply: error bars depict standard deviation. Added to description

Reviewer comment: Please provide error bars in figures 4 and 5.
Authors reply: Error bars (SD) added to figure 4. Data showed in figure 5 is same as figure 4.

Competing Interests: None

Reviewer Report 09 September 2022

https://doi.org/10.5256/f1000research.134894.r147805

Wiktor Jedrzejczak
World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw, Poland

General comments:
The manuscript is related to effects of coffee on contralateral suppression of transient evoked otoacoustic emissions (OAEs). The strengths of the manuscript are large group of subjects and the design with repeated measurements. However there are also several weaknesses like lack of information of the caffeine content used for the experiments and lack of any other verification of caffeine influence on the subjects besides OAEs, no comparison with previous studies, old and

wrong references to literature, very small references to OAE studies. My more specific comments are attached below.

Specific comments:

Introduction:
Several sentences in the introduction should be backed up by references, e.g.:

- "*In the cochlea, the OAEs are produced spontaneously and also in response to an external acoustic stimuli, referred as spontaneous OAEs and evoked OAEs respectively.*"

- *"The OAEs elicited in response to pure-tones are known as distortion product OAEs (DPOAEs) and stimulus frequency OAEs (SFOAEs)."*

- *"The suppression of OAE obtained by presenting noise to the non-test ear is known as the contralateral suppression of OAE.*"

The authors refer to review by Guinan, but he uses term of inhibition not suppression and it is directly stated why in the referenced paper. This should be at least commented.

Method:

- How much caffeine was in the coffee? Please provide information of the amount of caffeine used for the experiments.

- It would be good if the authors evaluated effect of coffee by some other test, to show that coffee influenced the subject at all, e.g. in studies of effect of attention on OAEs the attention level is evaluated by counting of stimuli or by evoked potentials, and then OAE analyses are made.

- How the authors evaluated the middle ear muscle reflex (MEMR)? Several studies point to MEMR interaction with experiments based on contralateral suppression of OAEs. The authors should check the MEMR influence or at least mention lack of it as the limitation of the study.

- Why are OAE parameters calculated by some program, and not taken from the ILO system?

- Provide some rationale for using 3 dB SNR criterion while studies of reliability of OAE suppression recommend using at least 6 dB or even more.

Results:

- Please provide error bars on figures 4 and 5.

- Maybe the authors could select smaller dataset with OAEs of SNR > 6dB?

Discussion:

- Study is based on TEOAEs so the comparisons to DPOAEs should be limited.

- Please compare results with other studies of suppression on same equipment, especially recent studies of reliability/variability. Even if there are no studies of coffee on suppression of OAEs, there are some studies of reliability of TEOAEs measured by the same equipment. These are very good basis for comparison, and for reference what change in TEOAE suppression would show the significant effect.

References:

- Please add references of some OAE review studies.
- Most references are old. Please add references for papers from last 5 years.
- There is in general too small number of references to OAE studies. There is plenty of OAE studies made on the same system with which the results could be compared.
- Mistakes – references to papers in which there is no referenced information. For example: "*Further, the OAEs elicited in response to short-duration stimuli such as clicks and tone-bursts are known as transient evoked OAEs (TEOAEs).*" which cites Kemp 1978. At this time Kemp did not used the name of TEOAEs.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: neuroscience, audiology, signal processing, otoacoustic emissions

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Author Response 01 Sep 2023

Mohan Kalaiah

We thank you for peer reviewing the manuscript.

Based on your recommendations, manuscript has been modified. See details below:

Introduction:
Reviewer comment: Several sentences in the introduction should be backed up by references, e.g.:
"In the cochlea, the OAEs are produced spontaneously and also in response to an external acoustic stimuli, referred as spontaneous OAEs and evoked OAEs respectively."
"The OAEs elicited in response to pure-tones are known as distortion product OAEs (DPOAEs) and stimulus frequency OAEs (SFOAEs)."
"The suppression of OAE obtained by presenting noise to the non-test ear is known as the contralateral suppression of OAE."
The authors refer to review by Guinan, but he uses term of inhibition not suppression and it is directly stated why in the referenced paper. This should be at least commented.
Authors reply: Citations added to the manuscript

Method:
Reviewer comment: How much caffeine was in the coffee? Please provide information of the amount of caffeine used for the experiments.
Authors reply: The caffeine content ranges from 2.2 to 3.1%. Thus, the amount of caffeine ranged from 27 to 40 mg per cup of coffee. Same information is added to the manuscript.

Reviewer comment: It would be good if the authors evaluated effect of coffee by some other test, to show that coffee influenced the subject at all, e.g. in studies of effect of attention on OAEs the attention level is evaluated by counting of stimuli or by evoked potentials, and then OAE analyses are made.
Authors reply: We agree with your recommendation, but other tests were not performed during the study. We acknowledge the same in discussion

Reviewer comment: How the authors evaluated the middle ear muscle reflex (MEMR)? Several studies point to MEMR interaction with experiments based on contralateral suppression of OAEs. The authors should check the MEMR influence or at least mention lack of it as the limitation of the study.
Authors reply: The middle ear muscle reflex was evaluated by measuring the acoustic reflex threshold for white noise. GSI Tympstar Pro immittance meter was used for measuring the reflex threshold for white noise. The lowest intensity at which a change in admittance was noted (referred as 'reflex threshold') was considered as an evidence of middle ear muscle reflex. In the present study the white noise was presented below the reflex threshold, during the measurement of contralateral suppression of TEOAE. Similar approach has been employed by several studies measuring the contralateral suppression of TEOAE.

Reviewer comment: Why are OAE parameters calculated by some program, and not taken from the ILO system?
Authors reply: During the study period, the computer used for recording and storing the OAE data failed. Data was not lost, as data files were copied to another computer. We could not find a way to load the data files back to ILO software platform for the purpose of data analysis. Thus, OAE parameters was calculated using EchoMaster software.

Reviewer comment: Provide some rationale for using 3 dB SNR criterion while studies of

reliability of OAE suppression recommend using at least 6 dB or even more.
Authors reply: We have reanalyzed the data and presented results using 6 dB SNR criterion.
Results:
Reviewer comment: Please provide error bars on figures 4 and 5.
Authors reply: Error bars (SD) added to figure 4. Data showed in figure 5 is same as figure 4.

Reviewer comment: Maybe the authors could select smaller dataset with OAEs of SNR > 6dB?
Authors reply: We have reanalyzed the data and presented results using 6 dB SNR criterion.

Discussion:
Reviewer comment: Study is based on TEOAEs so the comparisons to DPOAEs should be limited.
Authors reply: As studies related to TEOAEs are not available in literature, DPOAEs are cited for the purpose of comparison.

Please compare results with other studies of suppression on same equipment, especially recent studies of reliability/variability. Even if there are no studies of coffee on suppression of OAEs, there are some studies of reliability of TEOAEs measured by the same equipment. These are very good basis for comparison, and for reference what change in TEOAE suppression would show the significant effect.

References:
Reviewer comment: Mistakes – references to papers in which there is no referenced information. For example: “Further, the OAEs elicited in response to short-duration stimuli such as clicks and tone-bursts are known as transient evoked OAEs (TEOAEs).” which cites Kemp 1978. At this time Kemp did not used the name of TEOAEs.
Authors reply: Citation changed and error corrected

Competing Interests: No competing interests were disclosed.