Author's response to reviews

Title: Tone burst-evoked otoacoustic emissions in neonates: normative data

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Author's response to reviews: see over
A list of changes and/or rebuttal against each point

Reviewer #1: This report studies the properties of 1 kHz tone-burst OAEs in neonatal ears. This topic is timely because of the clinical importance of newborn hearing screening programs and limitations in existing transient-evoked OAE tests. The report will be of interest to OAE researchers.

- Minor Essential Revisions

**B1. Terminology:** The use of the term “stimulus intensity level” for peak-equivalent sound pressure level is incorrect. Sound intensity is a vector quantity that concerns the acoustic energy flow per unit area through a given surface.

The phrase “stimulus intensity level” has been modified to “stimulus level”.

**B2. Specific whether the target stimulus level was measured in each ear, or in some standard coupler or artificial ear.**

The target stimulus level is one of items in the ILO software settings. The operator can vary the target level setting and this allows the equipment to produce a stimulus level that should approximate the target at the eardrum. The actual sound pressure level usually is not exactly the same as the target level. The possible reasons are the types of probes, the acoustic characteristics of probes, and probe placement variations, as well as differences in individual ear canal sizes among neonates. The ILO equipment also gives information on the actual stimulus level produced in the ear for each recording and this data is also summarized in the Results section of the paper.

To avoid confusion, the statement has changed to “The Part II group comprised 705 ears, and the target stimulus level was fixed at 75 dB peSPL using the equipment software setting”. (See page 5 last two lines).

**B3. More discussion of why the 1 kHz tone burst mainly elicited a response near 1.5 kHz would be useful. This behavior was not observed in the Konrad-Martin and Keefe studies referenced below. If this outcome was due to spectral splatter from the two-cycle acoustic stimulus, windowing the electrical input stimulus might have been helpful. If this was due to increased noise at 1 compared to 1.5 kHz, and thus a reduced SNR at 1 kHz, it would be helpful to point that out. Given this result, would
it not be preferable to measure the TBOAE using a 1.5 kHz tone burst rather than a 1 kHz tone burst? The conjecture that some influence across TBOAE channels may have contributed to the frequency separation between response and stimulus energy is not well supported; this could be tested by high-level coupler measurements that product some distortion. It is not clear what intermodulation mechanism might produce this result.

The first paragraph on page 15 has been rewritten to incorporate the reviewer’s suggestions. Four possible reasons on why the SNR and prevalence rate in 1 kHz was lower than that at 1.5 kHz were discussed:

1. Increased noise at 1 compared to 1.5 kHz (supported by figure 4)
2. Filtering setting and “QuickScreen” mode in ILO system, which cut off some low frequency information.
3. Tone burst stimulus characteristics
4. The half octave display

The reason that the current results was not observed in the Konrad-Martin and Keefe studies may be because of the different recording instruments as well as different stimulus/recording parameters. In addition, it has been reported that mean SNR and the mean prevalence rate of CEOAE for 1 kHz frequency range are always lower than those for 1.5 kHz [1]. Therefore, the present study considered using 1 kHz TBOAEs (instead of 1.5 kHz center frequency) to elicit a more robust OAE response in the lower frequency region. We hope that this clarifies the issue.

**B4. A major conclusion is that combined 1 kHz TBOAE plus CEOAE measures may improve the pass rate in neonatal hearing screening programs. This conclusion must be tempered by reporting the total measurement time for each of these measures, and the extent to which the resulting pass rate would be superior to that using a CEOAE test alone with a long measurement time (equal to the total measurement time of the combination test).**

The present study did not report the comparison of test duration for each measure, as the main aim of this study was to provide 1 kHz TBOAE normative data, rather than determining the potential application in a neonatal hearing screening program. The related analysis of test duration has been published in another paper [1]. However, summary
information regarding mean test duration for 1 kHz TBOAE measurement has now been added in Result part II (page 11 third paragraph).

**B5. The “QuickScreen” mode should be described as a manufacturer’s term, and the critical property explaining its poor performance at 1 kHz is the fact that the window duration is too short in QuickScreen mode compared to the OAE latency at 1 kHz. This has been discussed by Hussain et al., *Ear Hear.* 19, 434-449, 1998.**

This is true that “QuickScreen” mode is a specific term in ILO system. So, the reference [13] was listed on page 6 last paragraph—the author of that paper was a key member for ILO system development. The sentence “CEOAEs were recorded using the ILO default ‘QuickScreen’ mode [13] for all study newborns” was also modified to incorporate the reviewer’s suggestion.

The reference paper (Hussain et al. *Ear Hear.* 19,434-449, 1998) is also cited on page 15, first paragraph to support our statement.

- **Discretionary Revisions**

**C1. Other studies on transient measurement of OAEs, which are analogous to TBOAEs, in older child and adult ears are Konrad-Martin and Keefe (*JASA* 114, 2021-2043, 2003; *JASA* 117, 3799-3815, 2005).**

These two articles are very useful. Thanks for the thoughtful suggestions.

**C2. Last two sentences of Procedures seem mixed up. If CEOAE and TBOAE test order was randomized, it doesn’t seem correct as well that ears passing CEOAE test were included in a subsequent TBOAE test.**

The last sentence on page 6 first paragraph has been rewritten to “The OAE test ear order for both CEOAE and TBOAE measures was random. All subjects initially had both CEOAE and TBOAE measures performed”. To make it more clear, an extra sentence-“Among the subject group, 745 CEOAE- and TBOAE-tested ears passed CEOAE hearing screening, and were included in the present studies.”- has also been added to the 'participants' part (page 5 last paragraph).
C3. On page 7, State the definitions of stimulus stability and reproducibility or provide reference.

A reference has been added on page 7 last paragraph.

C4. On page 8, it would be helpful to specify more description of the mother wavelet function that was proposed by Tognola. Was the Matlab 7.0 software standard Matlab or the Matlab Wavelet Toolkit? If the former, was the code developed in-house or provided by another researcher?

The Matlab 7.0 software we used is the standard Matlab. The mother wavelet function is used directly from Tognola’s publications [2, 3], while the complete code for program running was developed in-house. To make that more specific, one more equation has been added in page 8 third paragraph: “The mother wavelet function \( \psi(\cdot) \) used in this study was proposed by Tognola et al., which is a modulated cosine function \( \varphi(t) = (1/(1 + t^\beta)) \cdot \cos(\alpha \cdot t) \) [23, 24]. The time and frequency analysis of CEOAE signals have been shown to achieve the best results especially when \( \beta = 4 \) and \( \alpha = 20 \) are used [23, 24]”.

Reviewer #2:
-Major Compulsory Revisions

1. The first major problem with the present manuscript is that it seeks to propose pass criteria for infant screening without ever demonstrating that this criteria will indeed catch infants with hearing loss. Although it is not clear to me whether the specific procedure used here would catch infants with hearing losses, I have collected TBOAEs on listeners with cochlear impairment without difficulty at about 10-15 dB SL even when impairments at least as great as 50 dB HL are present. In other words, at test levels around 70 peSPL, you may actually get reasonably strong TBOAEs from fairly impaired ears. I do agree that it is likely that the SNR for these patients is likely to be lower than for normal ears, it is not clear to what extent this is the case without specific data answering this question.

The aim of this study was to explore the characteristics and the appropriate stimulus level of 1 kHz TBOAEs for those ears that have passed the CEOAE hearing screening. The
description of potential application of the combined TBOAE and CEOAE technique in neonatal hearing screening has been published in another journal paper [1].

It should be also acceptable that there are variable outcomes for TBOAE studies in different labs, since a variety of different instruments, stimulus and recording parameters, test environments and age/gender distributions may be employed. We hope that this clarifies the issue.

2. It is not at all clear to me that SNR is an appropriate criteria at all for passing or failing a screening. Using SNR as the criteria, infants who are noisy (fussy, breathing heavier, etc.) may fail despite their having the same OAE level (or an even greater one) as a quieter infant. Often, SNR is used to determine whether data collection has succeeded, but not necessarily as an assessment of the healthiness of the ear. Additionally, no clear information is given about the distribution of the OAE levels and the noise levels. We would have to know how likely it is for an infant to have a relatively low (but healthy) OAE and be noise enough to fail the +3 dB SNR criteria. We need two distributions--how many healthy ears will pass given the variability in noise and how many unhealthy ears will pass given the variability in noise--in order to decide whether this criteria is reasonable.

The SNR criterion has been commonly used in neonatal hearing screening field. This may because that the OAE signal has a very small amplitude, which is typically in the range of -20 to 20 dB SPL, so even if a signal level is lower (e.g. -5 dB), without the noise information, it is hard to say it should pass or fail. The relationship between noise and OAE response (or SNR) has been described as: “more than one octave band response which is 3 dB or more above the noise can be considered a significant result. If the noise level of say ‘X’ dB SPL exceeds the response the result is correct to say ‘OAE not detected’ and certainly less than ‘X’ dB SPL. It is incorrect to report ‘no OAE’ in noise conditions.” [4]. In addition, Otodynamics v6 software displays the response and noise in the same power spectrum. The signal and noise levels are calculated from the FFT of buffers A and B in the frequency domain, and the SNRs then are calculated from these frequency domain values. For the convenience of the user, the SNR value at each frequency band is finally shown on screen directly, which also makes the SNR value as a popular criterion in clinics throughout the world. Although band-limited reproducibility information has been also widely used as a
screening criterion, there actually is a relationship between SNR and reproducibility
calculation in ILO system. Hence the authors think that SNR information is of considerable
value, as it is a widely used clinical parameter.

It is true that infants who are noisy (fussy, breathing heavier, etc.) may fail despite their
having the same OAE level (or an even greater one) as a quieter infant. That is the reason
that some other indexes (e.g., stimulus stability, whole reproducibility) together with SNRs
should be all included as the suggested pass criteria (page 16 first paragraph).

3. Given these first two issues, I think it may be best to reframe these data as simply
some normative information on normal hearing infants’ TBOAEs without claims as
to how this information may be used for clinical classification. I believe that the data
are helpful and interesting, but not sufficient to justify specific clinical practice.

Some points in abstract, background and procedure part have been modified to
incorporate the reviewer’s suggestion.

The ears that used in TBOAE analysis were those that had passed the CEOAE hearing
screening, which means clinically they should be classified as normal hearing cases based on
current CEOAE-only pass criteria. The present study sought to explore the characteristics of
1 kHz TBOAEs obtained from such neonates, and then provide a reference for clinic and
research. As it is a reference, it was considered best to advise suggested criteria for
conducting TBOAE measurements. This study showed that supplementary information (e.g.
from improved SNR and hence OAE detection) in the lower frequency region could be
provided by 1 kHz TBOAE measurement, compared with the conventional CEOAE
measurements. However, the authors did not intend to claim that these TBOAE criteria
independently could be used to clinical classifications. The fairly cautious conclusion
highlights the researchers’ findings and the need for further research in this area.

4. Far too little information is given regarding the stimuli and the means of
measuring noise. There is no description of the windowing, averaging, binning, etc.
Without this information, it is difficult to determine what the results actually mean.
In particular, I have little understanding of your means for measuring noise based on
the manuscript.
In page 6 “Apparatus and parameters” section, the authors have mentioned the stimulus length, stimulus repetition rate, analysis window, stimulus levels, as well as the averaging information. The binning information has now been added in page 6 second paragraph.

Actually, the means of measuring noise/signal is auto-performed by ILO system or other current available clinical OAE system manufacturers, rather than users themselves. Therefore, most of stimulus and recorded parameters were set by default OAE systems, and they are not open to access by clinical researchers. Although there may have variables that differ slightly among different manufacturers, the authors believe the results still are of value as many clinicians use ILO equipment or equipment with similar parameters.

5. The brief tone burst used here (without windowing?) is going to generate a large amount of spectral spread. Please provide some information regarding the bandwidth of this spread and whether that is expected to affect the results. There is discussion regarding the improved frequency specificity of this stimulus over a click, but no quantification. Also, depending on the windowing, the RMS level will vary, which would be helpful to know for comparison with other work.

For the fixed tone pip stimulus length of 2ms in Otodynamics V6 software, the number of cycles (full wavelengths) will vary depending on the center frequency used. At 1000 Hz, the number of cycles is 2, and there is no setting for the plateau length. This information obtained by personal communication with ILO Company has already listed in page 6 last paragraph, but the exact bandwidth of tone pip stimulus spread in frequency domain is not available based on the current information.

It may also be a good point to include an RMS analysis in the time domain. However this index has not been provided directly by current manufacturers, and its inclusion here may not have much clinical meaning.

-Minor Essential Revisions

1. On Table 1, I am not certain what you mean by "Stimulus Repetition Rate." I assume this means the number of times per second the sound is presented. If this is the case, then Epstein and Florentine (2005) should be 12.2 rather than 50.

Thank you. This error has been corrected in the revised manuscript.
**-Discretionary Revisions**

1. *On Figure 2, the data are provided with error bars +/- 2 SEs. In this case, standard error tells us how sure you are regarding the group population mean. It is of much greater interest to the reader to know what the distribution of your population is. In other words, plotting with error bars that show +/- 1 standard deviation would give a clearer sense of the variability of individuals and whether this type of test is suitable as a screening tool. If the distribution is small, it makes an excellent test, if the distribution of the OAE levels and noise levels are very large, it is difficult to set very good criteria.*

   Thank you for this useful comment. This figure has been modified in the revised manuscript.

2. *I recommend caution when comparing prevalence rates across studies. The percentage of ears with OAEs present will vary wildly depending on the procedure used for making the measurements.*

   Yes. This is certainly true. Thanks the advice. This caveat has been noted.

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**References**


