The relationship between round window and ear canal Cochlear microphonic

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Abstract

Hypothesis: Cochlear microphonic recorded at ear canal (CM-EC) can be a substitute for the one recorded at round window (CM-RW).

Background: Almost all clinics do not measure tone-burst evoked CM due to technical difficulty although it can provide more information than click evoked CM. Moreover, clinicians like the CM-EC more than that measured at CM-RW because CM-EC is non-invasive. There is difference between CM-RW and CM-EC, for example, CM-EC is less prominent than CM-RW, therefore, studying tone-burst evoked CM-EC and its relationship with CM-RW are highly significant and can promote the clinical application of CM-EC.

Method: Nine guinea pigs were randomly allocated into three groups, group 1 was not exposed to noise, called normal control. group 2 and group 3 were exposed to the low- (0.5–2 kHz) and high-frequency band-noise (6–8 kHz) at 120 dB SPL for 1 h, respectively. It was difficulty to record low-frequency CM due to severe environmental interruption, in current study the recording technology of tone-burst evoked CM...
was optimized so that tone-burst evoked CM was measured across full speech frequency (0.5–8 kHz) in the presence of normal hearing and noise induced hearing loss (NIHL).

**Results:** CM-RW and CM-EC were successfully recorded across speech frequency. Significant reduction in CM amplitude was observed at 0.5 and 2 kHz in group 2, at 6 and 8 kHz in group 3 as compared to group 1, \( p < .05 \), indicating that CM amplitude was sensitive to band-noise exposure. Significant correlation between CM-RW and CM-EC was also verified, \( p < .05 \).

**Conclusion:** CM-EC is a useful objective test for evaluation of hearing function; the result of current study supports the clinical application of non-invasive CM-EC.

**KEYWORDS**

ear canal cochlear microphonic, noise induced hearing loss, round window cochlear microphonic

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### 1 | INTRODUCTION

Electrocochleography (ECoG) is widely used to evaluate cochlear function. Cochlear electrophysiological response includes cochlear microphonic (CM), summating potential (SP), resting potential (RP), and compound action potential (CAP); CM, SP, RP, and CAP are referred to as ECoG.\(^1^,^2\)

CM is adopted in current research because it is commonly used in clinical setting. CM recorded at round window (CM-RW) is very sensitive and accurate, but it is invasive, and can cause injury to patient.\(^3\) Non-invasive technology of ear canal recording of CM (CM-EC) seems to be a good substitute for CM-RW.\(^4^,^5\) However, the relationship between CM-RW and CM-EC has never been investigated, and the clinical application of CM-EC is limited.

Although click-evoked CM is commonly used in clinical setting, tone-burst evoked CM is not. Tone-burst evoked CM can provide frequency specific diagnosis of hair cell damage, and this is valuable for clinicians, as such diagnosis is important for clinical management.\(^6\) Sine tone-burst evoked CM across speech frequency has never been reported, tone-burst was used in current study to evoke frequency specific CM, and to investigate the relationship between CM-RW and CM-EC across speech frequency (0.5–8 kHz).

However, there is an issue in the measurement of low-frequency CM, the recording technology works well at high frequency,\(^7^,^8\) but works poorly at low-frequency (below 1 kHz or so) because of environmental interruption.\(^9\) Thus, a fundamental part of current study was the optimization of recording technology of CM, particularly at low frequency. After the technical difficulty of recording low-frequency CM had been solved, the first research goal of current study was to compare CM amplitude between normal control and noise exposure groups to investigate the sensitivity of CM of evaluation of hearing function in the presence of normal hearing and noise induced hearing loss (NIHL).

The second goal was to establish the response pattern of CM which could provide a direct illustration of auditory system function across speech frequency. The third and the most important goal was to investigate the relationship between CM-RW and CM-EC.

### 2 | METHODS

#### 2.1 | Animals

Guinea pigs with normal hearing as verified by the presence of Preyer’s reflex were used in the research. The animals were approximately 2 months old and weighed 250–300 g. All animal procedures were approved by the Animal Care and Use Committee, University of Alberta.

#### 2.2 | Instrument and noise exposure

Band pass filter was setup in Labview Signal Express (National Instrument) and used to generate band-noise. Low-frequency band-noise was set between 0.5–2 kHz, and high-frequency band-noise was set between 6–8 kHz. Nine animals were randomly allocated into three groups. Group 1 was not exposed to noise, called normal control. Group 2 and group 3 were exposed to the low- and high-frequency band-noise at 120 dB for 1 h, respectively.

#### 2.3 | Recording of Cochlear microphonic

The procedure used in our experiment was similar to that reported previously.\(^10^,^11\) Eaton-Peabody Laboratories Cochlear Function Test Suite (CFTS) was used to record CM. Animal was placed in a soundproof and electrically silent box. Room temperature was controlled at approximately 25°C. In each group, CM-RW and CM-EC were measured at 0.5, 2, 4, 6, and 8 kHz, respectively.

For the recording of CM-EC, a primary electrode was inserted subcutaneously in ear canal close to tympanic membrane. For the recording of CM-RW, a customized round window electrode was used, the electrode had a ball-shaped end that was fitted on round window.
In a mammalian brain, there are right and left auditory cortices, and each auditory cortex has independent selectivity of auditory signal. In a word, the two auditory cortices are functionally separated, and each auditory cortex has independent selectivity of auditory signal. Therefore, it is reasonable to consider the two ears in an animal are independent of each other.

However, considering the potential interaction between an animal’s two ears, we used the analysis of within subject effect of repeated ANOVA to test the interaction between an animal’s two ears. The result showed there was no significant interaction between an animal’s two ears, demonstrating the independence of an animal’s two ears in statistical analysis.

3 | RESULTS

3.1 | Research Goal 1: investigate the difference in amplitude of Cochlear microphonic as a function of noise induced hearing loss

The amplitudes of CM-RW and CM-EC were shown in Tables 1 and 2, respectively. Reduction in CM amplitude was noticed in groups 2 and 3 as compared to group 1, the change in CM amplitude between the three groups was analyzed by repeated measure of ANOVA.

Analysis showed main group effect at 0.5 and 2 kHz, respectively, \( p < .05 \) [(0.5 kHz CM-RW \( F_{(2, 3)} = 230.77 \) \[2 kHz CM-RW \( F_{(2, 3)} = 80.27 \) \[0.5 kHz CM-EC \( F_{(2, 3)} = 77.71 \) \[2 kHz CM-EC \( F_{(2, 3)} = 58.85 \)].

Bonferroni post hoc analysis was conducted to examine specific group difference. In term of the amplitudes of CM at 0.5 and 2 kHz, there was no significant differences between groups 1 and group 3, \( p > .05 \) [(0.5 kHz CM-RW \( F_{(1, 3)} = 2.19 \) \[2 kHz CM-EC \( F_{(1, 3)} = 2.16 \) \[0.5 kHz CM-EC \( F_{(1, 3)} = 1.38 \) \[2 kHz CM-EC \( F_{(1, 3)} = 0.63 \)].

The amplitudes of CM at 0.5 and 2 kHz in either group 1 or group 3 were significantly higher than those in group 2, respectively, \( p < .05 \) [(0.5 kHz CM-RW between G1 and G2 \( F_{(1, 3)} = 372.55 \) \[2 kHz CM-RW \( F_{(1, 3)} = 135.34 \); between G3 and G2 \( F_{(1, 3)} = 103.31 \) \[0.5 kHz CM-EC between G1 and G2 \( F_{(1, 3)} = 128.51 \); between G3 and G2 \( F_{(1, 3)} = 103.25 \) \[2 kHz EC between G1 and G2 \( F_{(1, 3)} = 95.40 \); between G3 and G2 \( F_{(1, 3)} = 80.51 \)]. The result indicated that low-frequency band-noise, caused specific reduction in the amplitudes of CM at 0.5 and 2 kHz.

At 4 kHz, no significant main group effect was noted between the three groups, \( p > .05 \) [(CM-RW \( F_{(2, 3)} = 0.872 \) \[CM-EC \( F_{(2, 3)} = 1.61 \); between G1 and G3 \( F_{(1, 3)} = 0.91 \); between G2 and G3 \( F_{(1, 3)} = 0.10 \) \[CM-EC between
G1 and G2 $F_{1, 3} = 0.31$; between G1 and G3 $F_{1, 3} = 0.25$; between G2 and G3 $F_{1, 3} = 0.00$).

At 6 and 8 kHz, significant main group effect were noticed respectively, $p < .05$ ([6 kHz: CM-RW and CM-EC $F_{1, 3} = 33.25$ and $24.17$, respectively, $p < .01$] [8 kHz: CM-RW and CM-EC $F_{1, 3} = 12.34$ and $25.02$ respectively, $p < .01$]). Bonferroni post hoc analysis showed, that in term of the amplitudes of CM at 6 and 8 kHz, there was no significant difference between group 1 and group

### TABLE 1  Amplitude of CM-RW

| Ear no. | 1    | 2    | 3    | 4    | 5    | 6    | Mean | SD   |
|---------|------|------|------|------|------|------|------|------|
| 0.5 kHz |      |      |      |      |      |      |      |
| Group 1 | 50.07| 49.10| 46.74| 48.08| 49.09| 48.39| 48.58| 1.13 |
| Group 2*| 19.15| 19.60| 21.63| 23.47| 20.66| 20.77| 20.88| 1.55 |
| Group 3 | 47.89| 49.87| 44.71| 43.66| 46.82| 45.76| 46.45| 2.24 |
| 2 kHz  |      |      |      |      |      |      |      |
| Group 1 | 38.04| 39.59| 36.34| 35.79| 37.45| 36.89| 37.35| 1.35 |
| Group 2*| 21.85| 22.63| 19.69| 17.96| 21.77| 21.03| 20.82| 1.72 |
| Group 3 | 32.69| 33.59| 34.49| 35.40| 36.32| 39.08| 35.26| 2.27 |
| 4 kHz  |      |      |      |      |      |      |      |
| Group 1 | 35.61| 35.60| 32.12| 33.80| 35.22| 34.89| 34.54| 1.36 |
| Group 2 | 33.19| 33.77| 30.80| 32.24| 35.18| 33.78| 33.16| 1.50 |
| Group 3 | 34.17| 34.74| 33.60| 31.12| 33.78| 33.62| 33.50| 1.24 |
| 6 kHz  |      |      |      |      |      |      |      |
| Group 1 | 31.86| 30.50| 28.71| 28.03| 29.94| 29.35| 29.73| 1.36 |
| Group 2 | 31.06| 29.04| 24.11| 25.61| 27.25| 27.33| 27.06| 1.94 |
| Group 3*| 16.10| 17.13| 15.05| 18.16| 21.14| 17.80| 17.01| 1.53 |
| 8 kHz  |      |      |      |      |      |      |      |
| Group 1 | 18.02| 19.23| 15.84| 14.98| 17.36| 16.63| 17.18| 1.92 |
| Group 2 | 16.59| 15.42| 13.23| 14.30| 18.01| 17.81| 15.89| 1.92 |
| Group 3*| 8.48  | 9.50 | 10.28| 10.87| 12.35| 11.34| 10.47| 1.37 |

Note: In 0.5 and 2 kHz panels, * indicates significant reduction in CM-RW amplitude at 0.5 and 2 kHz in group 2 as compared to that in group 1, $p < .05$. In 6 and 8 kHz panels, * indicates significant reduction in CM-RW amplitude at 6 and 8 kHz in group 3 as compared to that of group 1, $p < .05$. The CM-RW amplitude was in microvolt.

Abbreviations: CM-EC, Cochlear microphonic recorded at ear canal; CM-RW, Cochlear microphonic recorded at round window.

### TABLE 2  Amplitude of CM-EC

| Ear no. | 1    | 2    | 3    | 4    | 5    | 6    | Mean | SD   |
|---------|------|------|------|------|------|------|------|------|
| 0.5 kHz |      |      |      |      |      |      |      |
| Group 1 | 5.46 | 5.26 | 4.54 | 5.08 | 5.20 | 5.15 | 5.11 | 0.31 |
| Group 2*| 1.75 | 1.84 | 2.42 | 2.56 | 2.18 | 2.29 | 2.17 | 0.32 |
| Group 3 | 5.08 | 5.25 | 4.57 | 4.52 | 4.79 | 4.65 | 4.81 | 0.29 |
| 2 kHz  |      |      |      |      |      |      |      |
| Group 1 | 4.23 | 4.60 | 3.81 | 3.70 | 4.16 | 4.10 | 4.10 | 0.32 |
| Group 2*| 2.11 | 2.42 | 1.89 | 1.73 | 2.08 | 1.95 | 2.03 | 0.24 |
| Group 3 | 3.71 | 3.79 | 3.85 | 3.91 | 3.98 | 4.34 | 3.93 | 0.22 |
| 4 kHz  |      |      |      |      |      |      |      |
| Group 1 | 3.94 | 3.90 | 3.17 | 3.38 | 3.67 | 3.39 | 3.58 | 0.31 |
| Group 2 | 3.22 | 3.65 | 2.98 | 3.16 | 3.87 | 3.68 | 3.43 | 0.35 |
| Group 3 | 3.72 | 3.81 | 3.25 | 3.03 | 3.60 | 3.25 | 3.44 | 0.31 |
| 6 kHz  |      |      |      |      |      |      |      |
| Group 1 | 3.66 | 3.23 | 2.81 | 2.62 | 3.23 | 3.09 | 3.11 | 0.36 |
| Group 2 | 3.40 | 2.99 | 2.45 | 2.61 | 2.81 | 2.92 | 2.86 | 0.33 |
| Group 3*| 1.06 | 1.08 | 1.25 | 1.44 | 1.64 | 1.69 | 1.36 | 0.27 |
| 8 kHz  |      |      |      |      |      |      |      |
| Group 1 | 2.25 | 2.31 | 2.02 | 1.36 | 2.22 | 2.06 | 2.04 | 0.35 |
| Group 2 | 1.95 | 1.94 | 1.57 | 1.67 | 2.12 | 2.08 | 1.89 | 0.22 |
| Group 3*| 0.28 | 0.56 | 0.65 | 0.69 | 0.96 | 0.78 | 0.65 | 0.23 |

Note: In 0.5 and 2 kHz panels, * indicates significant reduction in CM-EC amplitude at 0.5 and 2 kHz in group 2 as compared to that in group 1, $p < .05$. In 6 and 8 kHz panels, * indicates significant reduction in CM-EC amplitude at 6 and 8 kHz in group 3 as compared to that of group 1, $p < .05$. The CM-EC amplitude was in microvolt.

Abbreviations: CM-EC, Cochlear microphonic recorded at ear canal; CM-RW, Cochlear microphonic recorded at round window.
2A and B shows the response patterns of CM-RW and CM-EC in group 1 respectively, indicating the highest amplitude of CM at 0.5 kHz, and the lowest amplitude at 8 kHz. In group 1, with the increment of frequency, the amplitude of CM had a tendency to decrease. Group 1 was not exposed to noise, and as such, the response pattern of CM shown in group 1 may reflect the standard characteristics of normal CM.

Figure 2C and D shows the response patterns of CM-RW and CM-EC in group 2, respectively. Reduction in the amplitude of CM was observed at 0.5 and 2 kHz in group 2 as compared to group 1. At other tested frequency, there was no difference in the response patterns of CM between groups 1 and 2.

Figure 2E and F shows the response patterns of CM-RW and CM-EC in group 3, respectively. Reduction in the amplitude of CM was observed at 6 and 8 kHz in group 3 as compared to group 1. At other tested frequency, there was no difference in the response patterns of CM between groups 1 and 3.

In summary, in group 1 the response pattern reflects the standard characteristics of normal cochlea; the comparison between the response patterns of CM in groups 1, 2, and 3, provides a direct illustration of frequency specific hearing loss induced by noise exposure.

3.2 | Research goal 2: establish the response patterns of Cochlear microphonic in the presence of normal hearing and noise induced hearing loss

In each group, mean and standard deviation of CM amplitude were plotted as function of the five tested frequencies to establish response pattern of CM.

In an individual group there were three animals (six ears), at each of the tested frequencies there were six recording of CM-RW and CM-EC, respectively. CM-RW and the CM-EC were considered as two continuous variables, Pearson’s correlation coefficient (PCC) was calculated to analyze the statistical correlation between CM-RW and CM-EC, and the correlation was considered significant when $p < .05$.

In each group, at each of the tested frequency there was strong correlation between CM-RW and CM-EC, $p < .05$. In a word, CM-EC correlated significantly with CM-RW in the presence of normal hearing and NIHL. PCC between CM-RW and CM-EC was shown in Table 3.

4 | DISCUSSION

4.1 | Frequency-specific cochlear damage

The findings of current study suggest that a band-noise exposure caused damage to a specific partition on cochlear basilar membrane. For example, the cochlear partition from 0.5 to 2 kHz was sensitive to the band-noise between 0.5 and 2 kHz, and the partition from 6 to 8 kHz was sensitive to the band-noise between 6 and 8 kHz.

Furthermore, the reduction in the amplitude of CM at 0.5 or 2 kHz of group 2, was larger than the reduction in the amplitude of CM at 8 kHz of group 3, respectively. These finding implies that low-frequency band-noise might cause more damages on outer hair cells (OHCs) than high-frequency band-noise did, so that larger reduction in the amplitude of CM at 0.5 or 2 kHz was observed in group 2. Our finding was consistent with other study, in which CM was found to be severely affected by low-frequency noise exposure.

4.2 | Mechanism about the reduction in Cochlear microphonic amplitude

In current study, reduction in CM amplitude was observed in noise exposure groups. The following is our explanation about the mechanism of CM amplitude reduction. CM is considered to be generated by OHCs, inner hair cells (IHCs) can also make contribution to the generation of CM. However, because the number of OHCs is much larger than that of IHCs, it is believed that CM is mainly generated by OHCs. And because noise exposure can induce damage and or death of OHCs, it is expected that CM amplitude will be reduced after noise exposure. However, the detail mechanism about damage and or death of OHCs is still unclear.

4.3 | The response pattern of Cochlear microphonic

CM amplitudes were plotted as function of tested frequencies to establish the response pattern of CM. An important characteristic was
noticed in the response pattern of CM in group 1, the highest amplitude of CM was observed at 0.5 kHz, when stimulus frequency went up, the amplitude of CM went down, with the lowest amplitude of CM at 8 kHz. Given that stimulus level was the same, the amplitude of CM evoked by high frequency stimulus was smaller than that evoked by low frequency stimulus.

Comparing to the response pattern of normal hearing shown in group 1, the response patterns after noise exposure shown in groups 2 and 3 indicate the frequency at which OHCs are sensitive to the damage of noise exposure. There are some discussion regarding the mechanism about response pattern of CM, but the mechanism is not clear.\textsuperscript{21–24}

4.4 | The correlation between Cochlear microphonic recorded at round window and Cochlear microphonic recorded at ear canal

The recording technology of CM can be classified into two classes, invasive and non-invasive methods. Invasive measurement of CM includes round window and trans-tympanic recording. Ear canal, mastoid and concha recording of CM are non-invasive measurements.

CM-RW in human during cochlear surgery, in which CM was recorded by a ball-shaped electrode placed on round window; in term of the reflection of hair cell function, CM-RW is the most sensitive method, and can yield the best signal noise ratio (SNR).\textsuperscript{25} However, round window recording is too invasive to be routinely used in clinic.\textsuperscript{26}

In trans-tympanic recording of CM, a primary needle electrode penetrates through tympanic membrane so that the electrode tip is as close to cochlear promontory as possible. One advantage of trans-tympanic recording is that its primary electrode is close to CM generator, OHCs, so the magnitude of CM recorded by trans-tympanic electrode is good. Although trans-tympanic recording of CM is less invasive, but this method can still cause injury and complication to patient, such as perforation of tympanic membrane and otitis media.\textsuperscript{27}

Recently there has been great interest in non-invasive recording of CM, such as ear canal recording, mastoid recording and concha recording.\textsuperscript{28,29} In ear canal recording, primary electrode is placed on skin surface that is close to tympanic membrane.\textsuperscript{30,31} Although the amplitude of CM-EC is about four times smaller than that by trans-tympanic recording, ear canal recording can be easily performed by an audiologist without any injury to patient, and it does not require a topical anesthetic which is needed in trans-tympanic recording.\textsuperscript{30,31}

CM can be measured by mastoid recording in which primary electrode is placed on skin surface of mastoid.\textsuperscript{4} It is noted that the amplitude of CM measured by mastoid recording is always smaller than that by ear canal recording,\textsuperscript{4} so CM-EC is more applicable in clinical setting that by mastoid recording.
The closer primary electrode is to the cochlea, the greater the amplitude of CM is.30

Thus, ear canal recording of CM offers a good and practical method between round window/trans-tympanic recording and other non-invasive method. The amplitude of CM-EC is smaller than that recorded by invasive method, but larger than that measured by other non-invasive approach. At the same time, CM-EC avoids injury and complication associated with round window/trans-tympanic recording.

In current study, CM-EC significantly correlates with CM-RW in the presence of normal hearing and NIHL, and the essential characteristics of CM waveform that are indispensable for diagnosis are preserved by ear canal recording, giving support for clinical application of CM-EC. Up to now, there have been no research in which CM-RW and CM-EC are recorded in the same subject, and no investigation about the correlation between them, as what we have done in current study.

5 | CONCLUSIONS

In term of the major contribution of current research, one is successful recording of tone-burst evoked frequency specific CM after optimization of recording technology, particularly 0.5 kHz CM. Furthermore, CM-RW and CM-EC were obtained and compared in the presence of normal hearing and NIHL, and the amplitude of CM was sensitive to noise exposure.

Click-evoked CM is currently available in clinic, however, tone-burst evoked CM is not. Tone-burst can generate a higher degree of frequency specificity of CM than click do, and stimulus duration of tone-burst is longer than that of click, the visualization of tone-burst evoked CM by is better than that evoked by click.32 Successful recording of tone-burst evoked CM across speech frequency is an important contribution of the current research.

The most important contribution of current study is the clarification of the strong correlation between CM-RW and CM-EC, which supports the clinical application of CM-EC.

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CONFLICTS OF INTEREST

We declare that there is no competing financial interests in relation to the work described. There is no conflict of interests.

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