

# [Editorial: new advances in electrocochleography for clinical and basic investigat...](https://assignbuster.com/editorial-new-advances-in-electrocochleography-for-clinical-and-basic-investigation/)

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Editorial on the Research Topic   
[New Advances in Electrocochleography for Clinical and Basic Investigation](https://www.frontiersin.org/research-topics/5083/new-advances-in-electrocochleography-for-clinical-and-basic-investigation)

Electrocochleography (ECochG) is a technique for recording evoked potentials from the inner ear, generally believed to originate from hair cells and nerve fibers. It is useful for assessing inner ear function in both laboratory and clinical settings. The abbreviation ECochG is preferable to ECoG, because the latter can be confused with “ electrocorticogram” ( [Ferraro, 1986](#B9) ). ECochG measurements are typically made from the ear canal or eardrum (extratympanic), from the promontory or round window niche (transtympanic), or from inside the cochlea (intracochlear). Extratympanic ECochG recordings are most commonly made with “ tiptrodes” (gold foil wrapped around insert earphones) or “ tymptrodes” (electrodes placed directly on the tympanic membrane). While the amplitude of tymptrode measurements can be up to an order of magnitude larger than tiptrode measurements ( [Ferraro and Ferguson, 1989](#B11) ), transtympanic amplitudes can be far more than an order of magnitude larger than those on the eardrum (e. g., [Ruth et al., 1988](#B40) ). We thus suggest that extratympanic measurements are best classified as far-field, and transtympanic measurements as near-field.

We will give a brief overview of ECochG before reviewing its traditional uses, and surveying recent advances that promise new applications in the assessment of auditory and vestibular function. References to the 23 papers collected for this Research Topic have been hyperlinked to Frontiers webpages. A more extensive historical overview of ECochG, including its basic features and applications, was provided by [Eggermont](https://doi.org/10.3389/fnsys.2017.00002) . A complementary review by [Gibson](https://doi.org/10.3389/fnins.2017.00274) offers tips for optimizing ECochG recordings in different clinical situations. Electrovestibulography (EVestG) is an analogous emerging technique for characterizing vestibular hair cell and nerve function, and was reviewed by [Brown et al.](https://doi.org/10.3389/fnsys.2017.00034)

Sensory cells of the inner ear can be manipulated, damaged, or destroyed in varying degrees depending on the ototoxic agent, administration approach, and dose, giving rise to hearing deficits at specific sound frequencies and intensities, as well as vestibular problems. A major long-term goal of ECochG is to help differentiate outer hair cell (OHC) from inner hair cell (IHC) or presynaptic losses, and from auditory nerve fiber (ANF) or postsynaptic losses, which are all presently lumped together as sensorineural hearing loss. Differential diagnosis of different forms of sensorineural hearing loss could prove useful in improving hearing aid fitting, in predicting cochlear implantation outcomes, and in individualized regenerative medicine ( [McLean et al., 2016](#B28) , [2017](#B29) ).

ECochG measurements are believed to originate, in general, from at least four distinct cellular sources, the receptor potentials of OHCs and IHCs, and the dendritic potentials and spikes of ANFs. The phases or polarities of these components can vary along the cochlea in a complex fashion that depends on stimulus characteristics and electrode placement, confounding their separation and interpretation ( [Chertoff et al., 2012](#B4) ). For example, the origins of the commonly measured summating potential (SP) and cochlear microphonic (CM) are still unknown for the wide range of stimulus parameters and recording locations. The older term “ cochlear response”, which seems to have become passé, thus remains an adequate descriptor of ECochG recordings as long as their origins remain elusive. A newer term with the same purpose appears to be the “ total response” (e. g., [McClellan et al., 2014](#B27) ). Continuing the progress toward untangling the different origins of ECochG measurements is essential to advance the clinical utility of ECochG (e. g., [Forgues et al., 2014](#B12) ; [Lichtenhan et al., 2014](#B23) ; Fontenot et al.).

The first ECochG measurements were obtained somewhat serendipitously by [Wever and Bray (1930)](#B49) , who were attempting to record from cat ANFs. Their alternating or AC potential would come to be known as the cochlear microphonic (CM) and its origin was attributed to the hair cells, primarily to the more numerous and sensitive OHCs ( [Dallos and Cheatham, 1976](#B6) ), which amplify and sharpen sound-induced vibrations before their detection by the sensory IHCs and ANFs. It was later discovered that ANF spiking could also contribute to CM measurements, particularly in response to lower-frequency sounds (< 1–2 kHz), and that IHCs contributed as well ( [Eggermont, 1974](#B8) ; [Chertoff et al., 2002](#B3) ; [Lichtenhan et al., 2014](#B23) ). This blend of responses became known as the auditory nerve neurophonic (ANN, e. g., [Snyder and Schreiner, 1984](#B46) ; [Forgues et al., 2014](#B12) ), which is simply a cochlear response to intense, low-frequency sounds. The Auditory Nerve Overlapped Waveform (ANOW; [Lichtenhan et al., 2013](#B22) , [2014](#B23) ) differs from the ANN in that it is evoked by low to moderate level sounds, and its cellular and spatial origins are known. ECochG measurements can be DC-biased by the summating potential (SP), and show compound action potential (CAP) responses to stimulus onsets and sometimes offsets, reflecting the synchronous spiking of ANFs ( [Davis et al., 1958](#B7) ; [Ruben et al., 1961](#B39) ). The CAP is wave I of the auditory brainstem response (ABR), first characterized by [Jewett and Williston (1971)](#B17) .

A long-standing use of ECochG has been to objectively corroborate a symptomatic and case-history diagnosis of endolymphatic hydrops in Meniere's disease and other pathological states (endolymphatic hydrops is not limited to Meniere's). In ears with endolymphatic hydrops, the SP/CAP ratio can be increased, due mainly to an increase in the SP, but also to a decrease in the CAP. Despite much research, it is not known whether the sensitivity and specificity of ECochG for detecting endolymphatic hydrops is high enough to be useful for individual patients. [Sass (1998)](#B43) reported high sensitivity and specificity (87 and 100%, respectively) when transtympanic click and 1 kHz tone burst SP/CAP ratios were combined with the increased CAP latency difference between rarefaction and condensation stimulus clicks that is also typical of ears with endolymphatic hydrops. Others have also reported good sensitivity and specificity by using the SP/CAP area (e. g., [Ferraro, 2010](#B10) ). As reviewed by [Eggermont](https://doi.org/10.3389/fnsys.2017.00002) and [Hornibrook](https://doi.org/10.3389/fnins.2017.00301) , the results of some other studies have been less encouraging, but there is consensus that tone burst ECochG presently yields the best results ( [Hornibrook](https://doi.org/10.3389/fnins.2017.00301) ). In a promising new approach, [Lichtenhan et al.](https://doi.org/10.3389/fnins.2017.00405) induced endolymphatic hydrops in guinea pigs using three classical manipulations and found that changes in the ANOW were more sensitive to small degrees of endolymphatic hydrops than were changes in traditional measures such as CAP thresholds and the endocochlear potential, suggesting that the ANOW could be useful in the early detection of endolymphatic hydrops.

ECochG can be used in the diagnosis of auditory neuropathy ( [Widen et al., 1995](#B50) ; [Rance and Starr, 2015](#B37) ), an umbrella term that includes many etiologies such as drug- or hypoxia-induced IHC loss ( [Harrison, 1998](#B14) ; [Salvi et al.](https://doi.org/10.3389/fnins.2016.00621) ), noise- and age-related synaptopathy ( [Kujawa and Liberman, 2015](#B19) ), hereditary synaptopathy and neuropathy (e. g., mutations of *OTOF, OPA1* , and other genes; [Santarelli et al., 2013](#B41) ), and even acoustic neuroma. While MRI can be useful in confirming some cases of auditory neuropathy (e. g., [Roche et al., 2010](#B38) ), it is typically diagnosed when an absent or abnormal CAP or ABR, even at high stimulus levels, co-occurs with a robust CM and/or otoacoustic emissions (OAEs). Speech perception deficits, both in quiet and in noise, are worse than expected from the audiometric loss. Identifying ears with auditory neuropathy is important for predicting cochlear implant outcomes, which are generally poorer compared to non-neuropathic patients ( [McMahon et al., 2008](#B30) ; [Walton et al., 2008](#B48) ; [Harrison et al., 2015](#B15) ; [Santarelli et al., 2015](#B42) ).

[Salvi et al.](https://doi.org/10.3389/fnins.2016.00621) provided an instructive review of selective IHC loss in chinchillas due to the cancer drug carboplatin. Substantial IHC loss had no measurable effect on OAEs or the CM (however, see [Chertoff et al., 2002](#B3) ), but reduced SP and CAP amplitudes. Tone thresholds in quiet were unaffected by IHC losses of up to 80%, but thresholds in noise were elevated ( [Lobarinas et al., 2016](#B25) ). Importantly, the chinchilla carboplatin studies reviewed by [Salvi et al.](https://doi.org/10.3389/fnins.2016.00621) were also among the first to provide compelling evidence for synaptic gain increases in the central auditory system in response to decreased peripheral input. While increased central gain can lead to improved audibility in quiet conditions (see e. g., [Hoben et al.](https://doi.org/10.3389/fnins.2017.00157) ), it might also lead to potentially bothersome tinnitus and hyperacusis ( [Noreña, 2011](#B31) ; [Schaette and McAlpine, 2011](#B44) ; [Pienkowski et al., 2014](#B34) ; [Brotherton et al., 2015](#B2) ; [Paul et al., 2017](#B32) ).

ECochG is a promising candidate for detecting noise- and age-related cochlear synaptopathy ( [Kujawa and Liberman, 2009](#B18) , [2015](#B19) ; [Sergeyenko et al., 2013](#B45) ). It was recently reported that college student musicians with normal audiometric thresholds up to 8 kHz, but mild hearing losses at 10–16 kHz, showed significantly increased click-evoked SP amplitudes and slightly decreased CAP amplitudes ( [Liberman et al., 2016](#B20) ), changes reminiscent of endolymphatic hydrops but in this case attributed to noise-induced synaptopathy. [Bramhall et al. (2017)](#B1) found reduced CAP amplitudes in military veterans with high noise exposure histories, and in non-veterans who reported a history of firearm use, compared with veterans and non-veterans with lower noise histories. Importantly, the reduced CAP amplitudes could not be explained by OHC dysfunction, as assessed with distortion product OAEs (DPOAEs). Other studies using CAP or ABR wave I amplitudes (as well as other metrics) have failed to detect evidence of synaptopathy in noise-exposed adults (e. g., [Prendergast et al., 2017](#B35) ). However, it may be that people who regularly subject themselves to high recreational noise doses do so because of their “ tougher” ears, which sustain less damage than the potentially more “ tender” ears of people who avoid loud music and noise (see e. g., [Henderson et al., 1993](#B16) for a general discussion of this issue).

[Grinn et al.](https://doi.org/10.3389/fnins.2017.00465) reported CAP and DPOAE amplitudes, and Words-in-Noise (WIN) performance in a group of young adults before, and 1 and 7 days after a loud recreational event, typically a concert (average dose of 93 dB A for 4 h, range 73–104 dB A for 1. 5–16 h). Consistent with the notion of tough vs. tender ears, there was no correlation between the noise dose and the amount of temporary threshold shift (TTS) measured across study participants. Most showed a 1 day TTS of < 10 dB (with full recovery at 7 days), accompanied by correspondingly small but significant temporary decreases in WIN scores. DPOAE amplitudes were affected at 1 day but only at 6 kHz, whereas CAP amplitudes to clicks and 2–4 kHz tone bursts were not affected. These results argue against the development of synaptopathy after a single recreational noise dose, consistent with laboratory noise exposure that caused a TTS in humans ( [Lichtenhan and Chertoff, 2008](#B21) ). It is likely that a number of such exposures is needed to produce permanent damage in primates ( [Pienkowski, 2017](#B33) ; [Valero et al., 2017](#B47) ).

To reduce the prevalence of noise-induced hearing loss, tinnitus, and hyperacusis, it would be helpful to identify those with especially tender ears. [Maison and Liberman (2000)](#B26) showed that the strength of the medial olivocochlear (MOC) efferent reflex in guinea pigs, as measured by the contralateral suppression of DPOAEs, was strongly correlated with lower TTS after acoustic trauma. Unfortunately, this finding has yet to be replicated in humans (e. g., [Hannah et al., 2014](#B13) ). [Smith et al.](https://doi.org/10.3389/fnins.2017.00189) made measurements of chirp-evoked human CAPs, confirming the original finding that chirps yield larger CAP amplitudes than clicks ( [Chertoff et al., 2010](#B5) ). [Smith et al.](https://doi.org/10.3389/fnins.2017.00189) found that CAP amplitudes were more strongly contralaterally suppressible than were DPOAE amplitudes, similar to the results of previous animal and human studies ( [Puria et al., 1996](#B36) ; [Lichtenhan et al., 2016](#B24) ). [Verschooten et al.](https://doi.org/10.3389/fnins.2017.00331) made progress in studying the human MOC reflex triggered by *ipsilateral* sound, by proposing how to separate MOC effects from the confounds of mechanical and neural masking.

This Research Topic reports innovations in recording techniques and signal processing that point to new potentially useful roles for ECochG in clinical practice ( [Charaziak et al.](https://doi.org/10.3389/fnins.2017.00169) ; [Cook et al.](https://doi.org/10.3389/fnins.2017.00472) ; [Kennedy et al.](https://doi.org/10.3389/fnins.2017.00429) ). Other innovations have noteworthy applications associated with cochlear implantation. [Bester et al.](https://doi.org/10.3389/fnins.2017.00141) , [Dalbert et al.](https://doi.org/10.3389/fnins.2018.00018) , [Koka et al.](https://doi.org/10.3389/fnins.2017.00210) , and [O'Connell et al.](https://doi.org/10.3389/fnins.2017.00291) , used ECochG to objectively assess residual, low-frequency acoustic hearing in ears implanted with hybrid electric-acoustic stimulation devices. [He et al.](https://doi.org/10.3389/fnins.2017.00339) comprehensively reviewed the electrically-evoked CAP or eCAP, including its applications in establishing implant candidacy, in intraoperative monitoring for electrode guidance, and in post-operative device programming and outcome assessment. [Riggs et al.](https://doi.org/10.3389/fnins.2017.00416) made intraoperative measurements from child and adult implantees with and without diagnosed auditory neuropathy, and found results consistent with better hair cell but poorer neural function compared to non-neuropathic patients. While it remains a challenge to accurately estimate ANF survival in implant candidates, [Pardo-Jadue et al.](https://doi.org/10.3389/fnins.2017.00395) suggest that tymptrode measurements of spontaneous ANF firing (in the absence of sound or other stimulation) could be helpful in this regard.

The telemetric innovations of modern cochlear implants have advanced research in intracochlear ECochG. [Kim et al.](https://doi.org/10.3389/fnins.2017.00216) reported the first intracochlear ECochG measurements from cochlear implant (Nucleus Hybrid L24) users. [Koka and Litvak](https://doi.org/10.3389/fnins.2017.00337) performed the first intracochlear ECochG recordings in response to simultaneous electrical and acoustic stimulation in patients implanted with Advanced Bionics HiRes 90K Advantage. The results of these pioneering measurements may point the way forward to objectively programming hybrid cochlear implants and better predicting speech outcomes.

The past informs the present, as the saying goes, and this is certainly true of the field of ECochG. It is usual for even good data to be misinterpreted in the context of the available theories of the day. Likewise, it is usual for previous interpretations to become outdated as new advances are made. Nevertheless, interpretations, not data, are typically the main intellectual drive of textbooks and review articles, and new trainees to a field often begin with these sources. Once a knowledge base becomes firmly entrenched, it can sometimes be difficult and uncomfortable to realize that a framework is no longer adequate to encapsulate new findings, and needs updating. We hope to have clarified some of the main ideas, terminology, and origins of ECochG measurements, and encourage all to study the almost 90 year history of this field.

## Author Contributions

MP: drafted the manuscript; JL and MP: edited the manuscript; JL: organized the Research Topic; JL, OA, and MP: shared editing responsibilities on the Research Topic.

## Conflict of Interest Statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Acknowledgments

We thank professors Jos J. Eggermont, James W. Hall III, and John J. Guinan Jr. for their productive comments on earlier drafts of this manuscript. We also thank professor Christoph Schreiner for helpful discussion on this work.

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