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ORIGINAL RESEARCH

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Stimulation conditions leading to electrical vestibular co-stimulation in cochlear implant users

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Abstract

Objectives: The study objective was to investigate the influence of electrical stimulus properties on cervical and ocular vestibular-evoked myogenic potentials to electrical stimulation by cochlear implants (e-cVEMPs, e-oVEMPs).

Methods: E-VEMPs were recorded in adult Nucleus cochlear implant (CI) patients using electric pulse trains (4 biphasic pulses at 1000 Hz burst rate). Ground path and stimulation electrodes were varied between monopolar stimulation at basal electrode contact E3 (MP1 + 2 E3), monopolar stimulation at apical electrode contact E20 (MP1 + 2 E20), and bipolar transmodiolar stimulation between E3 and E14 (BP E3-E14). The electric pulse train was further varied to 2 pulses at 1000 Hz, 2 pulses at 500 Hz, and a single pulse, in patients with present e-VEMP responses. VEMPs to bone-conducted vibration (BCV) were recorded as reference in all participants.

Results: Measurements were conducted in 30 ears of 27 participants (mean age 49.3 years, SD 12.7 years). E-VEMPs were present in 13 ears (43%). 5 of the 13 cases showed e-VEMPs but no BCV evoked VEMPs. Response numbers increased with increasing stimulation levels. The highest response rate of 40% was obtained for MP1 + 2 E3 stimulation. Stimulus variation did not affect response numbers. E-VEMP amplitudes were comparable to BCV-stimulated VEMPs. Latencies were up to 3.1 ms shorter for electric stimulation. Some patients showed e-VEMP thresholds close to or below the electric hearing threshold level.

Conclusion: The occurrence of e-VEMPs is dependent on current path and stimulation level. Vestibular co-stimulation by the CI is more likely in patients with high stimulation levels and for monopolar stimulation of basal electrode contacts.

Level of Evidence: 4.

KEYWORDS
cochlear implant, co-stimulation, electrical stimulation, VEMP, vestibular

1 | INTRODUCTION

Various clinical tests have been developed over the last decades to examine the contributors to posture and gait control in the vestibular system. The otolith integrity, more precisely the transient system (high-frequency response), can be examined by measuring cervical and ocular vestibular evoked myogenic responses (cVEMPs, oVEMPs).[1] VEMPs are clinically recorded as a response to high-intensity acoustical stimulation by air-conducted sound or bone-conducted vibration (BCV). Due to their vestibular origin, VEMPs can also be recorded in patients with profound sensorineural hearing loss or deafness. However, if sound conduction through the middle ear is impaired (conductive hearing loss)[2,3] or in patients with active implantable hearing devices,[4–6] BCV stimulation is required to elicit VEMPs.[7]

Another option to stimulate the otoliths is by electric currents, which elicit electrically evoked VEMPs (e-VEMPs). The three different approaches currently investigated are galvanic stimulation, direct stimulation by vestibular implant prototypes, and co-stimulation by cochlear implants (CIs).[8] The occurrence of CI co-stimulation is unintentially and most likely based on electrical current spread to the surrounding vestibular ganglion cells and/or vestibular nerve. In 1982, Eisenberg et al. investigated if currents delivered by the CI can improve postural stability.[9] Current spread in general is a known phenomenon, for example, leading to facial nerve co-stimulation as a rather common unintended side-effect in CI users[10] In case of electrical vestibular co-stimulation, the recording of CI evoked otolith-mediated reflexes can be performed as an objective measure of vestibular co-stimulation. Some studies investigated eye movements due to direct stimulation by a CI.[11,12] In other studies, e-VEMPs using direct electrical input via the CI were recorded.[13–15] Acoustic stimuli delivered through an audio processor, i.e., acoustic stimulation converted to electric stimulation, was used in another study[16] to elicit e-VEMPs. Other studies investigated the presence or absence of VEMPs, performing measurements with the CI off versus on and found no[17] or a positive effect of the CI[18–20] on VEMP response rates. In these studies, acoustic stimuli were presented through headphones without further specification of the position relative to the audio processor, i.e., differentiation between electric or acoustic stimulation.

This literature review shows major differences between e-VEMP response rates which are most likely attributed to methodological differences. The objective of this study was to determine e-VEMP response rates, amplitudes, latencies, and thresholds in Nucleus (Cochlear Ltd., Sydney, Australia) CI users for variations of ground path and electrical pulse trains.

2 | MATERIALS AND METHODS

2.1 | Study design and participants

A prospective explorative study was conducted between June 2020 and December 2021 at a single tertiary referral center and included patients between 18 and 65 years old with a Nucleus cochlear implant (Cochlear Ltd., Sydney, Australia) and perimodiolar electrode arrays. Patients with known vestibular disorders (e.g., vestibulopathy, Menière's disease, vestibular migraine), cochleovestibular schwannoma, cochlear malformation, electrode displacement, and cochlear fibrosis were excluded. The study protocol was reviewed and approved by the responsible institutional review board (approval number: 2020-22). Written informed consent was obtained from all participants.

2.2 | Experimental setup and procedures

VEMPs were recorded using the Eclipse recording system (Interacoustics A/S, Middelfart, Denmark). Details of the general recording procedure are described in Fröhlich et al. (2021).[7]

First, cVEMPs and oVEMPs were measured to 500 Hz BCV tone bursts (0-1-0) at 70 dB nHL using a B81 bone conduction transducer (Radioear, New Eagle, USA) at the mastoid tip ipsilateral to the CI side. Stimuli were presented at 8 Hz. The external CI audio processor was removed during the recording.

For electric CI stimulation, electric pulses were generated in the eABR module of Custom Sound EP software (version 6.0, Cochlear Ltd., Sydney, Australia). An external trigger signal was generated in the module and sent to the Eclipse via the CI programming pod. A distinct clinical CP910 audio processor (Cochlear, Sydney, Australia) was used for stimulus transmission to the implant.

The experimental procedure of e-VEMP recordings started with successive variations of the electric stimulus. Electric pulse trains were composed of biphasic pulses (25 μs pulse duration, 7 μs interphase gap) with a burst/stimulation rate of 1000 Hz, and burst duration of 3.057 ms (= 4 pulses at 1000 Hz). Stimuli were presented at 8 Hz. The ground path and stimulation electrodes were systematically varied between monopolar (MP) stimulation using both, the housing electrode and the external Ball electrode at the basal electrode contact E3 (MP1 + 2 E3), at the apical electrode contact E20 (MP1 + 2 E20), and bipolar (BP) transmodiolar stimulation between electrode contacts E3 and E14 (BP E3-E14).[21]

Only if an e-cVEMP and/or e-oVEMP could be recorded using one of these stimulation modes, the participant proceeded with the last part of the study. The electric pulse train was varied from the original 4 pulses at 1000 Hz to 2 pulses at 1000 Hz, 2 pulses at 500 Hz burst rate, and a single pulse using the ground path and stimulation electrode with the most reliable e-VEMPs recorded during ground path and stimulation electrode variation.

Before the e-VEMP recordings, the subjective electric hearing threshold (T-level) and maximum tolerable stimulation level (MTSL) were measured by subjective loudness scaling, i.e., asking the patient when the stimulus is just audible and when it cannot be tolerated to be any louder, for each of the different electric stimuli. All e-VEMP measurements were started at MTSL. If an e-VEMP could be recorded, the stimulus level was reduced in steps of 10 device-specific current levels (CL) until the threshold was reached.

TABLE 1 Characterization of study participants with respect to sex, age, implanted side, examined side in the study, implant type of examination side, duration of CI usage, and etiology leading to CI treatment.

ID	Sex	Age (years)	Implanted side	Examination side	Implant type	CI usage (months)	Etiology
1	M	59	R/L	R	CI512	104	Sudden idiopathic
2	F	42	L	L	CI512	41	Sudden idiopathic
3	M	60	R / L	L	CI24	90	Meningitis
4	F	61	R	R	CI512	44	Sudden idiopathic
5*	F	55	R / L	R*	CI24R	186	Unknown
6*	F	59	R	R*	CI24RE	94	Sudden idiopathic
7	M	36	L	L	CI632	2	Sudden idiopathic
8	F	54	R	R	CI632	1	Chronic otitis media
9	F	60	L	L	CI532	18	Genetic
10*	F	56	R	R*	CI24RE	145	Sudden idiopathic
11	F	47	L	L	CI532	26	Acoustic trauma
12	F	60	L	L	CI532	26	Sudden idiopathic
13*	M	20	R/L	R*	CI24RE	164	Unknown
14	F	43	L	L	CI532	41	Unknown
15	F	55	R	R	CI632	11	Chronic otitis media
16*	M	48	R / L	R*	CI24R	210	Labyrinthitis
17*	F	49	R	R*	CI632	4	Sudden idiopathic
18	F	60	L	L	CI632	12	Sudden idiopathic
19*	M	58	L	L*	CI512	77	Sudden idiopathic
20	M	35	R	R	CI512	52	Unknown
21*	M	35	R/L	L*	CI632	11	Miscellanous
				R*	CI632	1	
22	F	58	R/L	R	CI632	17	Sudden idiopathic
				L	CI532	25	
23*	F	24	R	R*	CI24RE	107	Meningitis
24*	F	63	R / L	R*	CI512	64	Unknown
				L	CI532	29	
25*	F	23	R/L	R*	CI632	16	Genetic
26	F	63	R/L	R*	CI24RE	157	Sudden idiopathic
27	M	47	R	R	CI532	26	Unknown

Abbreviations: M, male; F, female; L, left; R, right; *, e-VEMP response present.

2.3 | Data analysis

The VEMP data were analyzed in OtoAccess software (Interacoustics A/S, Middelfart, Denmark). For cVEMPs, the amplitude was normalized to the tonic muscle activation.

VEMP analysis was performed by two blinded examiners. To assess the inter-rater reliability the intraclass correlation coefficient (ICC) was calculated in a two-way mixed model for single measures and absolute agreement for the e-cVEMP and e-oVEMP amplitudes. If no responses could be detected, the amplitude was set to 0 (cVEMPs) or 0 µV (oVEMPs) for this statistical test. Inter-rater agreement was considered "poor" for ICCs below 0.50, "moderate" between 0.50 and below 0.75, "good" between 0.75 and 0.90, and "excellent" above 0.90.[22] Good or excellent agreement was considered acceptable for further analysis. The final amplitudes and latencies were the averages of the examiners' ratings.

VEMP response rates were reported as absolute number of e-VEMP responses (response number) and analyzed with respect to the MTSL which was applicable in the patients. The influence of stimulus variation on the e-VEMP response number was analyzed for e-cVEMPs and e-oVEMPs using the Chi-square test. Descriptive statistics were used to report VEMP latency, amplitude, and threshold data. For threshold analysis, the e-VEMP thresholds were corrected for the respective T-level, i.e., analyzed as difference between e-VEMP threshold and T-level. Quantitative data were presented as mean, standard deviation (SD), and range (minimum and maximum).

SPSS statistics (IBM, Armonk, New York, USA) was used for all statistical analyses. A confidence level of 95% or above was

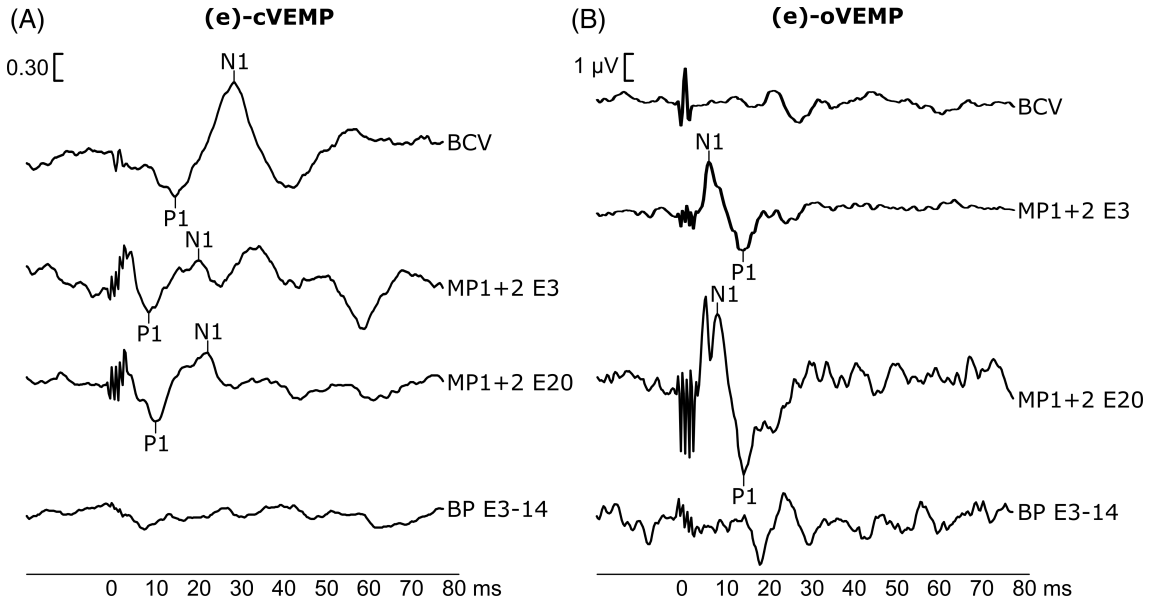

FIGURE 1 Representative (e-)cVEMP and (e-)oVEMP waveforms (ID 17) to stimulation by BCV and electric stimulation. The CI stimulation artifacts are visible at 0 ms.

considered to be significant (p <.05). If appropriate, qualitative data were presented as graphs using GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA).

3 | RESULTS

The study sample included measurements in 27 (9 male and 18 female) patients with a mean age of 49.3 years (SD: 12.7 years, range 24–63 years). Table 1 shows an overview of the study population. The mean experience with the CI was 60 months (SD: 147 months). Study measurements were conducted in a total of 30 ears (cases).

The inter-rater reliability analysis by ICC revealed excellent agreement between the two raters for both, (e-)cVEMP and (e-)oVEMP amplitudes. For (e-)cVEMPs, the single measure ICC was 1.0 with a 95% confidence interval from 0.99 to 1.00 [$F(35) = 4655.73$, p< .001]. For (e-)oVEMPs, the single measure ICC was 0.999 with a 95% confidence interval from 0.998 to 1.0 [$F(27) = 2514.82$, p <.001].

3.1 | Number of (e-)VEMP responses

Figure 1 displays representative VEMP recordings to BCV and electric stimulation. In total, VEMPs to BCV were measured in 22 cases (73%). In 13 cases, both cVEMPs and oVEMPs could be recorded, 7 showed only cVEMPs and 2 only oVEMP responses. Electric stimulation, regardless of stimulation mode elicited VEMP responses in 13 cases (43%). E-cVEMPs and e-oVEMPs could be recorded in 5 cases, 4 showed only e-cVEMPs, and 4 showed only e-oVEMPs. In 8 of the 13 cases with e-VEMPs, both BCV and electric stimulation elicited a VEMP response. In 5 of the 13 cases, only e-VEMPs were recorded but no VEMPs to BCV stimulation.

Figure 2A shows the number of e-VEMP responses for variation of stimulus ground path using the electric pulse train consisting of 4 pulses at 1000 Hz. The highest response number of 12 cases was obtained for MP1 + 2 E3. For MP1 + 2 E20, e-VEMPs were recorded in 3 cases, and to bipolar stimulation (BP E3-E14), e-VEMPs could be elicited in 7 cases. The Chi-square test revealed no statistically significant influence of stimulus ground path on e-cVEMP or e-oVEMP response numbers (p >.05). However, the data showed a clinically significant trend of higher e-VEMP response numbers when basal electrodes were stimulated, especially in monopolar mode.

All except one participant with e-VEMPs showed a response to MP1 + 2 E3 stimulation. Only one participant (ID 21), had an e-oVEMP response to bipolar stimulation and 4 pulses at 1000 Hz but not to any other stimulation modality and no e-cVEMPs on the left side. However, patient ID 21 was measured bilaterally and e-VEMPs were present to monopolar stimulation on the right side. Thus, the left side was excluded from further analysis and 12 cases were included in the analysis of the last part of the study. Figure 2B shows the absolute e-VEMP response numbers for varying electric pulse trains and MP1 + 2 E3 stimulation based on the results from the ground path variation (see Figure 2A). Reducing the number of pulses led to a minor reduction of the number of responses. E-VEMPs were obtained for 2 pulses at 1000 Hz in 9 cases, for 2 pulses at 500 Hz in 9 cases, and for stimulation with a single pulse in 7 cases. The effect of variation of electric pulse train with respect to burst rate and the number of pulses was not statistically significant in the Chi-square test (p >.05).

Figure 3 shows the absolute e-VEMP response numbers in dependence of the MTSL that could be applied during the study measurements. Low MTSL between 140 and 179 CL did not elicit an

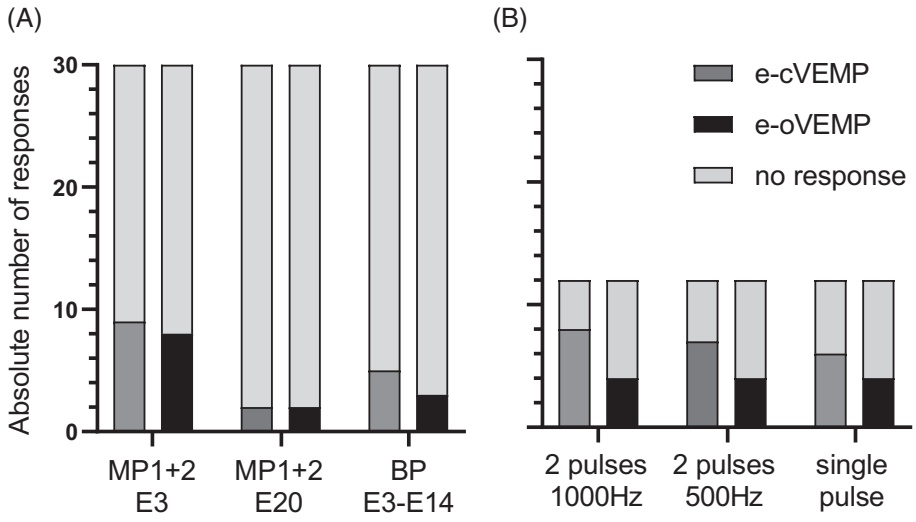

FIGURE 2 Absolute e-cVEMP and e-oVEMP response numbers for different stimulation modalities. (A) Variation of stimulus ground path between monopolar stimulation at E3 (MP1 + 2 E3) or E20 (MP1 + 2 E20) and bipolar stimulation at E3 and E14 (BP E3-E14) using the electric pulse train consisting of 4 pulses at 1000 Hz. (B) Variation of electric pulse trains with 2 pulses and 1000 Hz, 2 pulses and 500 Hz, and single pulses using MP1 + 2 E3 stimulation based on the results from the first part.

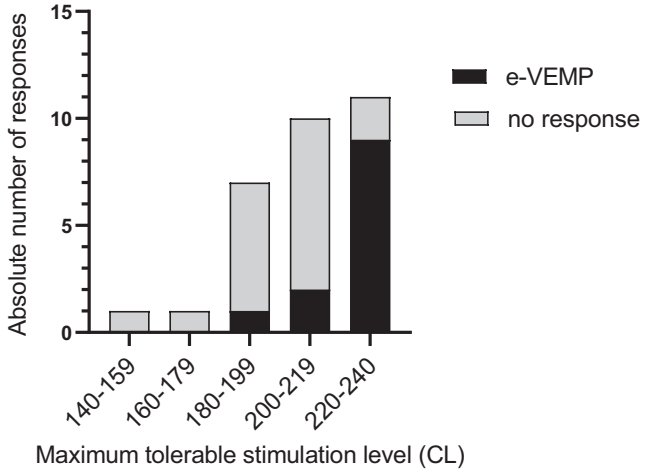

FIGURE 3 Absolute e-VEMP response numbers in dependence of the MTSL which could be applied during the study measurements.

e-VEMP response. The lowest MTSL that elicited an e-VEMP response was between 180 and 199 CL. The e-VEMP response number increased with increasing tolerance for stimulation level and had a maximum of 220–240 CL. While the response rate for the group of patients with MTSL between 200 and 219 CL was 20%, it increased to 82% in the MTSL range between 220 and 240 CL, which was considered a clinically highly significant difference.

3.2 | Amplitudes and latencies

The amplitudes for (e-)cVEMPs and (e-)oVEMPs are illustrated in Figure 4. Cases without responses, i.e., amplitudes of 0 or 0 μV, are not included. The amplitudes for stimulation by BCV are illustrated as reference. For cVEMPs, the mean amplitude to BCV stimulation was 0.8 (SD: 0.4, $n = 20$). The maximum mean e-cVEMP amplitude to electric stimulation was 1.0 (SD: 0.8, $n = 9$), obtained for MP1 + 2 E3. For monopolar apical and for bipolar stimulation, the amplitudes were lower. The number of pulses and frequency did not have an effect on the e-cVEMP amplitudes. For oVEMPs, the mean amplitude to BCV stimulation was 6.3 μV (SD: 7.4 μV, $n = 15$). Amplitudes for monopolar electric stimulation were comparable to BCV stimulation. Bipolar electric stimulation resulted in the lowest mean e-oVEMP amplitude of 3.4 μV (SD: 1.8 μV, $n = 3$). The e-oVEMP amplitudes decreased with a reduction of the number of pulses and frequency.

Figure 5 shows the (e-)cVEMP and (e-)oVEMP latencies with reference to stimulation by BCV. For cVEMPs to BCV stimulation, the mean p13 latency was 11.6 ms (SD: 1.9 ms, $n = 20$) and the mean n23 latency was 23.3 ms (SD: 2.9 ms, $n = 20$). To electric stimulation, the mean e-cVEMP latencies were approximately 2 ms shorter with a mean p13 latency of 13.9 ms (SD: 1.3 ms, $n = 36$) and a mean n23 latency of 21.2 ms (SD: 1.77 ms, $n = 36$) over all stimulus variations. No difference was observed between latencies for ground path and stimulus variations. BCV evoked oVEMPs showed a mean n10 latency of 9.6 ms (SD: 1.5 ms, $n = 15$) and a mean p15 latency of 14.1 ms (SD: 2.0 ms, $n = 15$). To electric stimulation in monopolar mode, the e-oVEMP latencies were comparable to BCV stimulation. Longer latencies with a mean n10 latency of 10.7 ms (SD: 1.5 ms, $n = 3$) and a mean p15 latency of 14.8 ms (SD: 0.8 ms, $n = 3$) were observed in bipolar mode. Varied stimulation to 2 pulses at 1000 Hz as well as single pulses showed approximately 1 ms shorter latencies compared to BCV stimulation.

3.3 | Thresholds

The e-cVEMP and e-oVEMP thresholds corrected for the individual T-levels are shown in Figure 6. Thresholds had a wide range between −15 CL to 100 CL. The smallest variation was observed for MP1 + 2 E3 stimulation. The highest thresholds were obtained with MP1 + 2 E20 stimulation with a mean threshold of 88 CL (SD: 18 CL) for e-cVEMPs and 85 CL (SD: 21CL) for e-oVEMPs. For all other stimuli, the mean thresholds were between 39 CL and 60 CL, showing no clinically significant effect of ground path and stimulus variation on

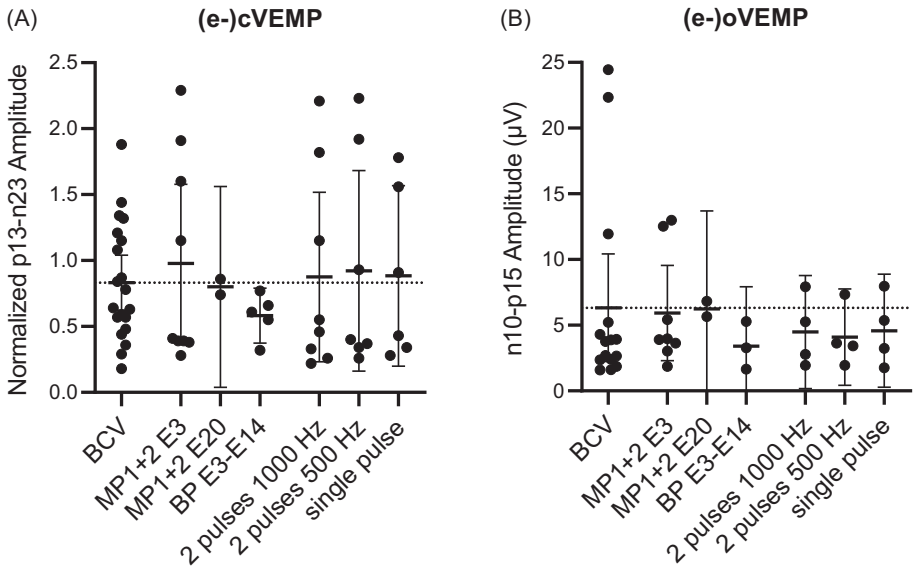

FIGURE 4 Amplitudes with means and 95% confidence intervals for BCV evoked VEMPs and e-VEMPs for the different stimulation modalities. Cases without responses, i.e., amplitudes of 0 or 0 µV, are not included. The dotted lines show the mean amplitudes for BCV-evoked VEMPs as reference. (A) (e-)cVEMPs and (B) (e-)oVEMPs.

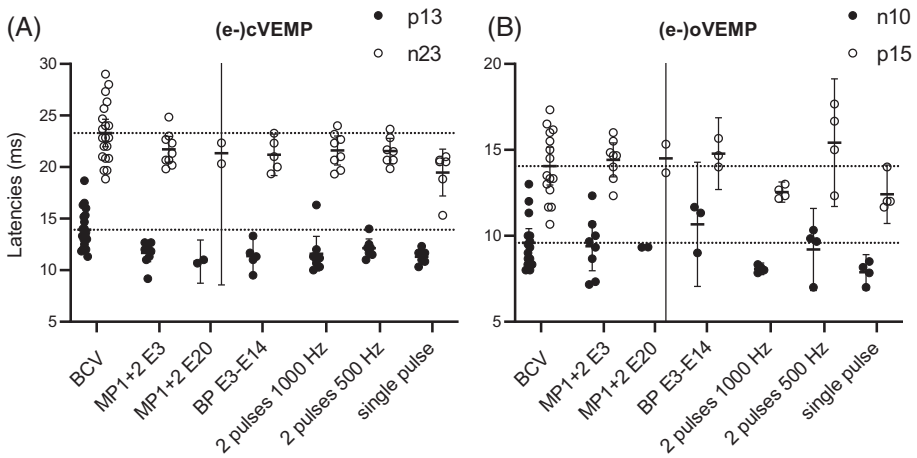

FIGURE 5 Latencies with means and 95% confidence intervals for BCV evoked VEMPs and e-VEMPs for the different stimulation modalities. The dotted lines show the mean latencies for BCV-evoked VEMPs as reference. (A) (e-)cVEMPs and (B) (e-)oVEMPs.

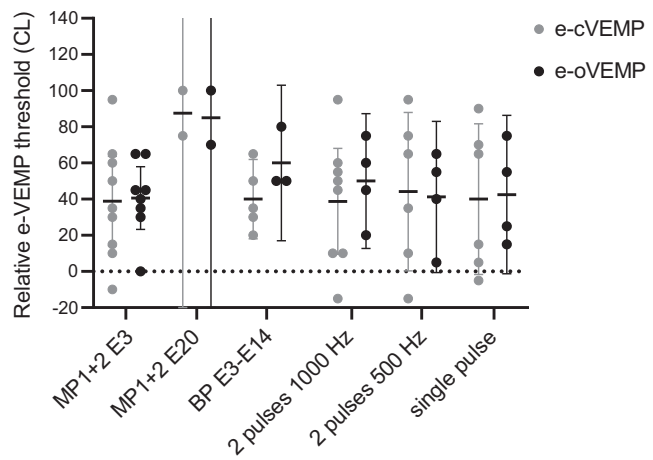

FIGURE 6 E-cVEMP and e-oVEMP thresholds with means and 95% confidence intervals for the different stimulation modalities. Thresholds are indicated as differences to the individual respective T-levels, i.e., relative thresholds.

normalized e-VEMP thresholds. Some participants showed thresholds at very low stimulation levels close to or exactly at T-level, for example, ID 10 and ID 13. In one participant, ID 5, e-VEMP thresholds were below T-level, i.e., below electric hearing threshold.

4 | DISCUSSION

Vestibular co-stimulation is a known but only insufficiently investigated side effect in CI treatment most likely based on electric current spread. Three studies investigated the occurrence of vestibular co-stimulation by the recording of CI evoked e-VEMPs. These studies used different stimulation modalities, i.e., ground path, stimulation electrodes, stimulus frequencies, and other stimulus parameters, and reported different response numbers. This is the first study to systematically vary the electric stimulus delivered by the CI with respect to ground path and stimulation electrode as well as the electric stimulus itself, i.e., stimulus frequency (burst rate) and the number of pulses per stimulus.

The absolute response rate regardless of stimulation modality was 43%, which is lower than the 58% response rate reported by Parkes et al.[14] However, Parkes et al. included only pediatric and young adult patients which could explain the difference as lower response numbers for VEMPs can generally be observed with increasing age.[23] In the study by Basta et al.,[13] only e-cVEMPs were recorded and the response rate was 100%. Different from our study, the recordings were conducted intraoperatively under general anesthesia so that patient discomfort was not a limiting factor and high stimulation levels could be applied. Rodriguez Montesdeoca et al.[15] reported e-cVEMPs from intraoperative recordings in 1 of 4 patients but the stimulation level in their study was limited to 180 CL. The generally strong influence of the stimulation level on the e-VEMP response number was confirmed in our study that considered response numbers with respect to the individual MTSL in CI patients during e-VEMP testing. The results are in line with the observations by Parkes et al.[14] and showed a clinically significant increase of response numbers with increasing MTSL.

The variation of stimulation modality did not show a statistically significant effect. However, the highest response numbers were obtained for monopolar stimulation at the basal electrode E3 with a clinically significant difference compared to monopolar apical stimulation and bipolar stimulation. This is in line with the literature where monopolar stimulation resulted in higher response numbers than bipolar stimulation.[13] Monopolar stimulation results in a longer current path length and is associated with more current spread, i.e., a larger electric field, compared to bipolar stimulation where the current path is more locally restricted in the cochlear. Thus, vestibular co-stimulation is more likely to occur in monopolar mode. Regarding the stimulation location, i.e., apical versus basal, similar trends were also reported in other studies.[14,15] The proximity between basal electrodes and the vestibular structures could make vestibular co-stimulation more likely. The electric currents are most likely to travel through the fluid along the scala and leave the cochlea at the base, for example, through the round window.[24]

Amplitudes of e-VEMPs were found to be comparable to BCV-evoked VEMP amplitudes for those stimulation modalities that were identified as effective, especially MP1 + 2 E3. However, latencies differed between electric and BCV stimulation. Particularly for e-cVEMPs, the latencies were approximately 2 ms shorter compared to BCV stimulation. Shorter latencies for electric stimulation were also reported in the literature.[13–15] This implies that electric stimulation of the vestibular system is faster compared to BCV stimulation, possibly bypassing the otoliths and stimulating vestibular ganglion cells and/or the vestibular nerve directly. This should apply for saccular as well as utricular afferents. However, an effect could not be observed for e-oVEMPs in this study.

E-VEMP thresholds were investigated with respect to T-level, i.e., the electric hearing threshold. A wide range of thresholds was observed and some patients showed e-VEMPs close to or even below T-level. In practice, this means that vestibular co-stimulation occurred when the electric stimulus was barely audible or not audible at all. Thus, vestibular co-stimulation is very likely to occur in these patients during daily life CI use.

Vestibular function in CI users can be impaired postoperatively due to damage of vestibular structures[25] but the functional impact of CI vestibular co-stimulation has not been examined so far and should be investigated in future studies.

Due to practical considerations, the study was limited to Nucleus cochlear implants and perimodiolar electrode arrays. However, the occurrence of vestibular co-stimulation by the CI is most likely based on technical and anatomical factors that influence the spread of the electrical field. Thus, future studies should also investigate the effect of electrodes, especially straight (lateral wall) electrode arrays, on e-VEMPs. To investigate the relation between current spread and the occurrence of vestibular co-stimulation e-VEMP response numbers should be analyzed in dependence of current spread measures, for example, transimpedance or spread of excitation measurements.

5 | CONCLUSION

The study showed the feasibility of recording e-VEMPs as a measure of electrical vestibular co-stimulation in Nucleus CI users. Vestibular co-stimulation by the CI is likely in patients with high stimulation levels and for monopolar stimulation of basal electrode contacts. It can occur during daily CI use in clinical fitting maps.

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CONFLICT OF INTEREST STATEMENT

The institution of the authors (1) receives grant money for other research projects from Cochlear Ltd., Sydney, Australia, and MED-EL, Innsbruck, Austria.

DATA AVAILABILITY STATEMENT

The data of this research project are available on reasonable request from the authors.

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