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Simultaneous recording of cervical and ocular vestibular-evoked myogenic potentials

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Abstract

Objective
To increase clinical application of vestibular-evoked myogenic potentials (VEMPs) by reducing the testing time by evaluating whether a simultaneous recording of ocular and cervical VEMPs can be achieved without a loss in diagnostic sensitivity and specificity.

Methods
Simultaneous recording of ocular and cervical VEMPs on each side during monaural stimulation, bilateral simultaneous recording of ocular VEMPs and cervical VEMPs during binaural stimulation, and conventional sequential recording of ocular and cervical VEMPs on each side using air-conducted sound (500 Hz, 5-millisecond tone burst) were compared in 40 healthy participants (HPs) and 20 patients with acute vestibular neuritis.

Results
Either simultaneous recording during monaural and binaural stimulation effectively reduced the recording time by ≈55% of that for conventional sequential recordings in both the HP and patient groups. The simultaneous recording with monaural stimulation resulted in latencies and thresholds of both VEMPs and the amplitude of cervical VEMPs similar to those found during the conventional recordings but larger ocular VEMP amplitudes (156%) in both groups. In contrast, compared to the conventional recording, simultaneous recording of each VEMP during binaural stimulation showed reduced amplitudes (31%) and increased thresholds for cervical VEMPs in both groups.

Conclusions
The results of simultaneous recording of cervical and ocular VEMPs during monaural stimulation were comparable to those obtained from the conventional recording while reducing the time to record both VEMPs on each side.

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Glossary

ACS = air-conducted sound; **cVEMP** = cervical vestibular-evoked myogenic potential; **HP** = healthy participant; **oVEMP** = ocular vestibular-evoked myogenic potential; **SCC** = semicircular canal; **VEMP** = vestibular-evoked myogenic potential; **VN** = vestibular neuritis.

Introduction of vestibular-evoked myogenic potentials (VEMPs) has enabled easy assessment of the otolithic function in clinical practice.[1–4] Cervical VEMPs (cVEMPs) reflect the function of the vestibulo (sacculo)–spinal pathways,[5] while ocular VEMPs (oVEMPs) evaluate the integrity of the vestibulo (utriculo)–ocular pathways.[6–9] In contrast to cVEMPs, which represent an ipsilateral inhibitory vestibulospinal response, oVEMPs examine a crossed excitatory vestibulo-ocular reflex.[10] Therefore, evaluation of both oVEMPs and cVEMPs permits assessment of both otolithic end organs, inferior and superior vestibular nerves, and the vestibulo-spinal and vestibulo-ocular pathways in the brainstem at once.[4,11] Although each VEMP test (cVEMP and oVEMP) by itself has an acceptable duration of <1 hour, conducting both VEMPs in addition to other vestibular function tests definitely increases the whole testing time. Moreover, it can be very wearing for patients with acute vestibular syndrome or elderly patients to conduct all these tests in 1 long session while enduring a load of acoustic stimuli. Therefore, shortening the recording time and acoustic stimuli and enhancing cooperation would increase the feasibility of VEMP testing.

Although several studies have adopted bilateral simultaneous stimulation in healthy participants (HPs) and patients with vestibular disorders to reduce the diagnostic procedure for recording VEMPs,[12,13] there have been no systematic, crossover, controlled, head-to-head comparison studies between the conventional and simultaneous recordings within the same group of HPs or patients. In the current study, we evaluated the feasibility of the 2 different methods of simultaneous recording of VEMPs compared to the conventional sequential recordings in HPs and in patients with acute vestibular neuritis (VN).

Methods

Study design

This is a single-center, randomized, 3-way crossover study design. A crossover trial involves 3 different sessions of cVEMP and oVEMP measurements that are arranged in a random order on different days with 1- or 2-day intervals among the test conditions (figure e-1, http://links.lww.com/WNL/A46). Three different sessions included the conventional sequential recording and 2 different simultaneous recording methods, i.e., unilateral simultaneous recording of cVEMP and oVEMP during monaural stimulation (figure 1A, Sm) and bilateral simultaneous recording of each VEMP during binaural stimulation (figure 1B, Sb). All recordings were performed by the same examiner,[14] and the required time for each testing was measured after the exclusion of the time required for evaluating thresholds, preparing the participants, and attaching the electrodes.

As a feasibility trial to show the absence of difference in VEMP parameters, we calculated an overall minimum sample size of 30 participants from power analysis.[15]

Participants

Participants, regardless of sex, at least 18 years of age were eligible for the trial from March to August 2016. Those with a history of vertigo or neuro-otologic diseases and abnormal findings in pure tone audiogram and head-impulse tests were excluded.

Participants with acute, severe, prolonged vertigo associated with spontaneous nystagmus, postural imbalance, nausea, or vomiting were enrolled. The inclusion criteria as a patient with VN involving the superior division included the following: (1) acute vertigo that was (2) associated with horizontal and torsional nystagmus, (3) impaired horizontal semicircular canal (SCC) function on video head-impulse test and a unilaterally absent or reduced caloric response (i.e., horizontal SCC gain <0.50 and a caloric paresis score >25%), and (4) the absence of auditory and neurologic signs. We also enrolled patients who showed involvement of the inferior vestibular division with the below criteria in addition to the above superior VN criteria (mixed superior and inferior VN): (5) the appearance of downbeat or torsional nystagmus and (6) unilaterally impaired posterior SCC function on video head-impulse test (i.e., posterior SCC gain <0.70). We performed imaging studies in patients with downbeat nystagmus to exclude intracranial lesions. All patients were tested in the acute stage of the disease within 10 days of symptom onset.

HPs and patients were pseudorandomized in an equal ratio of orders to receive each recording method (figure e-1, http://links.lww.com/WNL/A46).

cVEMP and oVEMP recording

Conventional sequential cVEMP and oVEMP recording

To record cVEMPs, participants were placed in the supine position and asked to raise their head ≈30° from the bed and rotate it contralaterally to reliably activate the sternocleidomastoid muscles. An active surface EMG electrode placed over the belly of the ipsilateral sternocleidomastoid and a reference electrode on the incisura jugularis of the sternum

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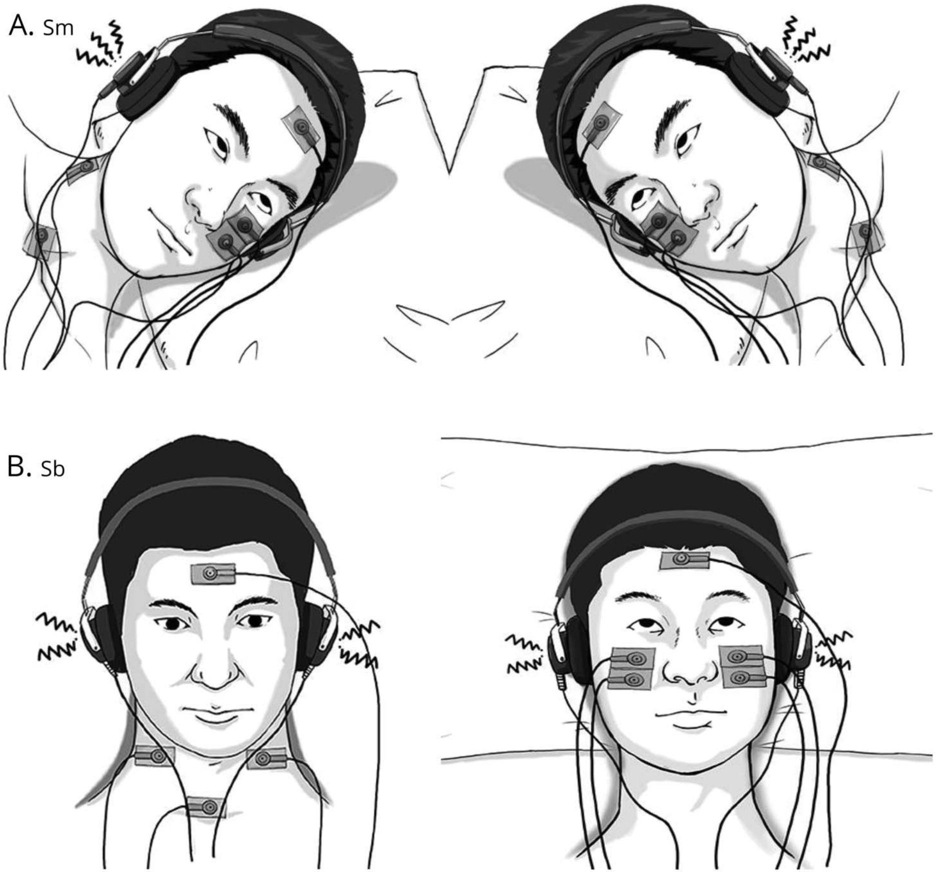
Figure 1 Illustrations of the simultaneous VEMP recording methods



(A) Left, for unilateral simultaneous recording of cervical vestibular-evoked myogenic potentials (cVEMPs) and ocular VEMPs (oVEMPs) during right ear stimulation, the participants were supine on a bed with their heads raised ≈30° from the horizon and rotated leftward. During recording, the subject looked ≈25° upward with sound stimulation of the right ear. Active electrodes were placed over the belly of the right sternocleidomastoid muscle for the cVEMP test and ≈1 cm inferior to the lower eyelid of the left eye for the oVEMPs. The reference electrodes were attached to the incisura jugularis of the sternum for the cVEMPs and ≈2 cm below the ocular active electrodes for the oVEMPs. The ground electrode was placed on the forehead. Right, a similar configuration was used for unilateral simultaneous recording of the left side. (B) Left, for bilateral simultaneous recording of the cVEMPs, active electrodes were placed on the bilateral middle third of sternocleidomastoid muscles, the reference electrode was placed on the incisura jugularis of the sternum, and the ground electrode was placed on the forehead. Participants were instructed to keep the head elevated while in the supine position, and short tone bursts acoustic stimuli were delivered binaurally through a headphone. Right, for recording oVEMPs bilaterally, active electrodes were placed below the eyelids bilaterally and the reference electrodes were below the active electrodes while the participant maintained an upward gaze during binaural sound stimulation. The ground electrode was placed on the forehead.

with self-adhesive Ag/AgCl electrodes were used for the recording.[16,17] For the recording of oVEMPs, the active electrode was located on the infraorbital ridge below the center of the contralateral lower eyelid, and the reference electrode was placed below the active electrode.[16] During monaural sound stimulation, participants were asked to fix their gaze on the target located ≈25° above straight ahead.

Differential amplifiers (bandwidth 10–2,000 Hz) were used, and the unrectified signals (n = 100) were averaged (Cadwell Laboratories, Kennewick, WA).[17] We used unilateral 500-Hz, 5-millisecond air-conducted sound (ACS) tone bursts with the stimulation delivered from an intensity of 100-dB normal hearing level after calibration.[17] Amplified EMG potentials were bandpass filtered at 10 to 3,000 Hz, and then the data were averaged from the stimulus onset to 50 milliseconds. To provide adequate levels of EMG activation and to ensure fine adjustment of the head position, we controlled the participants to match the EMG levels for each side, to allow measurement of background contractibility, and to calculate the normalized peak-to-peak amplitudes.[17]

Each participant was evaluated for VEMP thresholds by reducing 5-dB stimulus intensities in steps over successive trials, and the smallest intensity with a VEMP producing in at least 2 trials was defined as a threshold.

Unilateral simultaneous cVEMP and oVEMP recording

In this simultaneous recording method, cVEMPs and oVEMPs were recorded at the same time unilaterally with monaural sound stimulation (figure 1A). During the right ear stimulation, an active electrode was located at the belly of the right sternocleidomastoid, and a reference electrode was placed on the sternum for cVEMPs. For oVEMPs, the active and reference electrodes were placed on the left lower eyelid. The participants were then asked to lift and turn their head to the left side and to look up at the target above straight ahead during right ear stimulation (figure 1A, left). Then, recording of cVEMPs and oVEMPs on the opposite side was conducted in a similar fashion; the active and reference electrodes were on the opposite sides with the head lifted and turned to the right and an upward gaze during left ear stimulation (figure 1A, right). The same target was located straight upward 25° to prevent the eye from being more adducted and elevated, which makes the greater inferior oblique muscle contract and have a larger amplitude. To match the muscle contraction for each side, the EMG levels were monitored as in the conventional method.

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Bilateral simultaneous recording of each VEMP

The other simultaneous recording method is bilateral simultaneous recording of cVEMP or oVEMP with binaural acoustic stimulation (figure 1B). To record cVEMPs on both sides, the active electrodes were located at the middle of the bilateral sternocleidomastoid muscles, and the reference electrode was attached on the incisura jugularis.[18] During recording, participants were instructed to keep their head elevated in a supine position without turning the head as in the previous condition, and short-tone-burst acoustic stimuli were delivered binaurally (figure 1B, left). During bilateral cVEMP recording (figure 1B, left), the contractibility of the sternocleidomastoid was smaller compared to the contractibility during monaural cVEMP recording (figure 1A) (mean sternocleidomastoid contractibility by EMG recording 55 vs 95 μV). To record oVEMPs bilaterally, the active and reference electrodes were placed on both sides of the cheeks while the participant was looking up during binaural sound stimulation (figure 1B, right).

Statistical analysis

The coprimary endpoints were that there are no significant differences in the mean time for each recording and the parameters of each VEMP, including p13 and n10 latency, peak-to-peak amplitudes, asymmetry ratio, and threshold of cVEMP and oVEMP between conventional separate recordings and each simultaneous recording.

Analysis of variance tests were used to compare the mean test time and parameters between conventional and simultaneous recordings. A statistical significance was defined as $p < 0.05$. The SPSS version 20 statistical software (IBM Corp, Armonk, NY) was used.

In this study, we did not compare the VEMP parameters between the HP and patient groups because it was not the main topic of this study. Furthermore, the ages were different between the 2 groups (mean age 33.1 years in HPs vs 63.5 years in patients). As age increases to >60 years, the VEMP response decreases markedly with a decrease in the amplitude and an increase in the latency, and these were also observed in the current study.[19,20]

Standard protocol approvals, registrations, and patient consents

This study was approved by the Institutional Review Board at Chonbuk National University Medical School, and informed consents were obtained from all participants. The clinical trial identifier number assigned by ClinicalTrials.gov was NCT03049683.

Results

Forty HPs (age 23–46 years, mean age 33.1 years, 25 male) participated in this study, and 20 patients (age 47–77 years, mean age 63.5 years, 12 males) fulfilled the criteria of VN. Two patients (51 and 66 years old) with spontaneous downbeat nystagmus in addition to horizontal nystagmus showed caloric paresis and impaired horizontal and posterior SCCs function with the head-impulse tests. They were diagnosed as having mixed superior and inferior divisional VN.

Recording time for each method

We compared the mean required time for each VEMP recording method on both sides, excluding the time for the threshold test, preparation, and attaching the electrodes. Compared to the conventional sequential recordings, the unilateral simultaneous recording with monaural stimulation shortened the test time by 48% and 62.4%, and bilateral simultaneous recordings with binaural stimulation reduced it by 56.5% and 52.6% for both VEMPs in HP and VN group, respectively ($p < 0.001$, tables 1 and 2). In HPs, the mean required test time for unilateral simultaneous recording of cVEMP and oVEMP was 8.7 minutes for 1 side and therefore 17.4 minutes for both sides. This was significantly shorter than the total test time of ≈33 minutes for both cVEMPs and oVEMPs with conventional unilateral recordings (table 1).

VEMP parameters of the HP group

In 40 HPs, during the conventional recordings of cVEMP and oVEMP, the responses from each ear did not differ (table 1).

The unilateral simultaneous recording of cVEMPs and oVEMPs on each side during monaural stimulation revealed that the p13 latency and peak-to-peak amplitude of cVEMP and the n10 latency of oVEMP did not differ compared to conventional recordings (figures 2 and 3). However, the peak-to-peak amplitudes of oVEMPs were larger than those from the conventional recording on both sides ($p = 0.04$ and $p = 0.003$, respectively, table 1 and figure 3B). The cVEMPs and oVEMPs were symmetric between the sides with asymmetry ratios of ≈24%, and the thresholds for cVEMPs and oVEMPs were similar to the values obtained with separate recordings.

During the bilateral simultaneous recordings, there were no significant differences in oVEMP parameters, including the mean thresholds, compared to the conventional recordings of oVEMP. However, the peak-to-peak amplitudes of the cVEMP were significantly lower compared to the conventional separate recordings on each side without asymmetry ($p < 0.001$, table 1 and figure 3A). In addition, the cVEMP thresholds during bilateral simultaneous recordings (figure 2E) were significantly higher compared to those of conventional recordings (figure 2D) ($p < 0.001$, table 1).

VEMP parameters of patients with VN

In patients with VN, the parameters of oVEMPs showed asymmetric responses with markedly reduced or absent n10 components beneath the eye opposite the affected ear during the conventional recording ($p = 0.02$, table 2 and figure e-2B, http://links.lww.com/WNL/A46). In contrast, the mean parameters of cVEMPs did not differ between the affected and unaffected ear stimulation (table 2 and figure e-2A). In

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Table 1 Comparison of parameters of VEMPs of healthy participants during simultaneous cVEMP and oVEMP recordings on each side with monaural stimulation and simultaneous recordings of each VEMP during binaural stimulation vs conventional sequential recording in response to 5,000-Hz ACS tone burst

oVEMPs	n10 Latency, mean ± SD, ms		*p* Value[b]	Amplitude, mean ± SD, μV		*p* Value[b]	AR, %	Threshold, dB nH		Total test time, min[c]
	Right	Left		Right	Left			Right	Left	
Conventional recording	12.5 ± 1.4	12.1 ± 1.2	0.30	5.4 ± 3.9	5.0 ± 3.3	0.58	23.0 ± 17.0	84.5 ± 5.8	84.3 ± 7.1	14.8 ± 3.4
Monaural simultaneous	12.1 ± 0.9	12.5 ± 0.9	0.11	7.6 ± 3.5	8.6 ± 2.7	0.37	24.2 ± 16.7	84.7 ± 5.9	84.5 ± 6.5	8.7 ± 1.1[d] (48%)[e]
p Value[a]	0.30	0.12		0.04	0.003		0.77	0.60	0.56	<0.001
Binaural simultaneous	12.9 ± 1.1	12.5 ± 1.0	0.17	4.9 ± 3.7	5.2 ± 3.6	0.38	15.1 ± 11.9	83.6 ± 6.2	84.3 ± 5.9	8.4 ± 1.6 (57%)[e]
p Value[a]	0.3	0.12		0.20	0.66		0.06	0.12	1.00	<0.001

cVEMPs	p13 Latency, mean ± SD, ms		*p* Value[b]	Amplitude, mean ± SD, μV		*p* Value[b]	AR, %	Threshold, dB nH		Total test time, min[c]
	Right	Left		Right	Left			Right	Left	
Conventional recording	15.6 ± 0.8	15.7 ± 1.1	0.64	504.4 ± 246.6	442.4 ± 239.4	0.15	19.3 ± 13.8	75.3 ± 4.4	75.1 ± 4.9	18.1 ± 2.9
Monaural simultaneous	15.1 ± 1.2	15.2 ± 0.6	0.63	507.7 ± 208.7	505.2 ± 178.5	0.97	24.4 ± 14.5	75.7 ± 3.8	75.9 ± 4.2	8.7 ± 1.1[d] (48%)[e]
p Value[a]	0.14	0.09		0.96	0.27		0.33	0.62	0.17	<0.001
Binaural simultaneous	15.8 ± 1.1	15.9 ± 1.3	0.68	142.9 ± 86.1	146.4 ± 80.1	0.83	18.0 ± 11.9	83.9 ± 7.4	83.3 ± 6.3	10.2 ± 2.1 (56%)[e]
p Value[a]	0.42	0.42		<0.001	<0.001		0.72	<0.001	<0.001	<0.001

Abbreviations: ACS = air-conducted sound; AR = asymmetry ratio; cVEMP = cervical vestibular-evoked myogenic potential; nH = normal hearing; oVEMP = ocular vestibular-evoked myogenic potential.
p Values by paired *t* test or Wilcoxon signed-rank test for trends as appropriate.
[a] *p* Value compared to conventional sequential recordings.
[b] *p* Value comparing the right and left values.
[c] The mean required time for VEMPs on both sides excluding the time for preparation, attaching the electrodes, and the threshold test.
[d] Required test time for cVEMPs and oVEMPs on 1 side.
[e] Compared to the conventional sequential recordings, shortened percent of the test time during simultaneous recordings.

individual analysis, 2 patients with downbeat nystagmus and abnormal head-impulse test on the posterior in addition to the horizontal SCC revealed low p13 amplitudes of cVEMP on the affected side.

Unilateral simultaneous recording with monaural stimulation presented delayed latencies and reduced/absent n10 amplitudes (p = 0.01, table 2 and figure e-2C, http://links.lww.com/WNL/A46) of oVEMPs on the affected side as in the conventional recordings. In contrast to the conventional separate recordings, the parameters of cVEMPs on the affected side revealed decreased mean amplitudes (p = 0.003, table 2), which reflect the results of decreased cVEMP amplitudes in the patients who had an involvement of the inferior division. When we recalculate the mean amplitude of cVEMPs after removing the 2 patients with involvements of the inferior vestibular nerve, there is no statistic difference in the amplitudes between the affected and unaffected sides (106.7 ± 69.2 vs 237.4 ± 83.3 μV, p = 0.17).

During bilateral simultaneous recording, the n10 amplitude (oVEMP) of the affected ear was decreased or absent (p = 0.02, table 2 and figure e-2E, http://links.lww.com/WNL/A46). The p13 amplitude of cVEMP was significantly decreased on both sides (p = 0.001, table 2 and figure e-2D), which was observed also in the HPs, and was even more decreased on the affected side (p = 0.03, table 2). The latencies of cVEMPs and oVEMPs did not show significant differences between the affected and unaffected sides during bilateral simultaneous recordings with binaural sound stimulation.

Discussion

This study demonstrates that simultaneous recordings with either monaural or binaural stimulation can effectively reduce the time required for testing both cVEMPs and oVEMPs on both sides. Reducing the testing time with simultaneous recordings also has a further important advantage of applying only half of the acoustic stimulations. The sound intensities of

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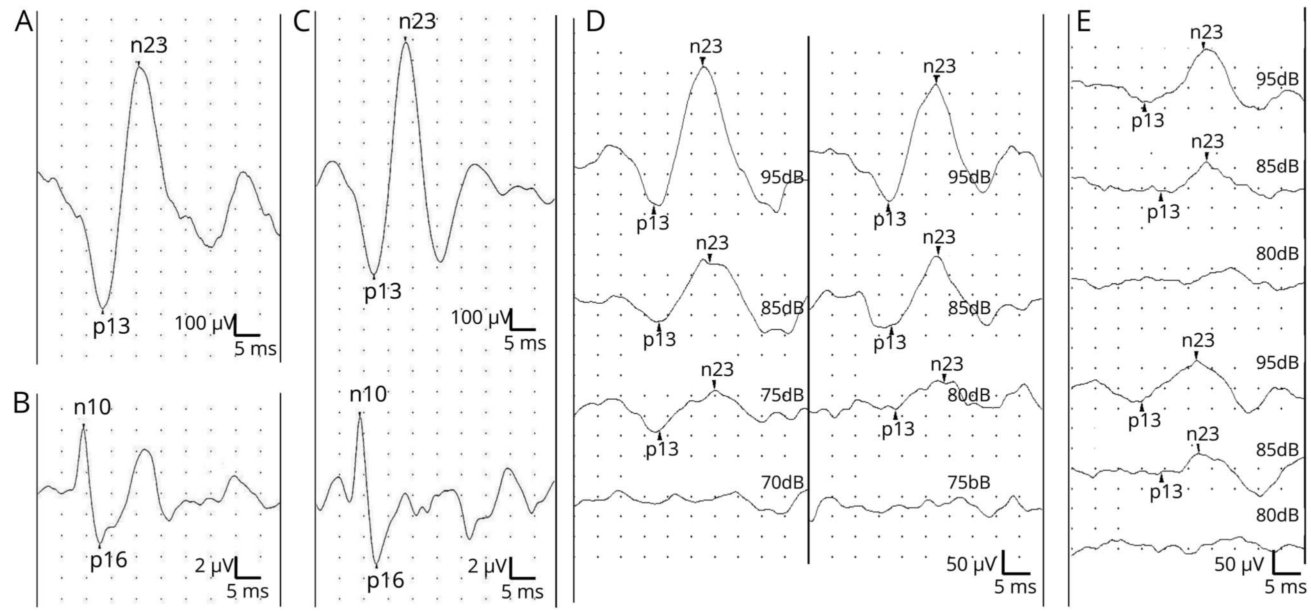
Figure 2 VEMPs of a representative normal subject (28-year-old man) produced by sound stimuli of 5-millisecond tone bursts at 500 Hz during the conventional and simultaneous recordings



(A) Conventional separate recording of cervical vestibular-evoked myogenic potentials (cVEMPs) on the right side showed that peak latency of p13 was 13.2 milliseconds and the peak-to-peak amplitude was 1,154 μV. (B) The conventional recording of ocular VEMPs (oVEMPs) revealed the peak latency of n10 at 9.9 milliseconds and the amplitude at 10.8 μV. (C) Unilateral simultaneous recordings of the cVEMPs and oVEMPs during the right monaural stimulation show the latency of p13 at 13.3 milliseconds and amplitude of 1,032 μV and the latency of n10 of oVEMPs at 10.0 milliseconds and amplitude of 14.2 μV, which was recorded on the left eye. (D) Threshold testing of cVEMPs in each side during conventional separate recording and (E) during bilateral simultaneous recordings with binaural stimulation revealed that the peak-to-peak amplitude of cVEMPs during bilateral recording was significantly decreased compared to the separate recording and the thresholds of cVEMPs during bilateral simultaneous recording were higher compared to those of conventional recordings.

impulse noise during routine VEMP recordings (100- to 110-dB normal hearing level, 10 milliseconds, 200–300 repetitions) may potentially harm the inner ear and affect hearing.[5,11,21,22] Therefore, reducing the testing time and muscle contraction would be safer and more comfortable for patients with acute vestibular disorders or for elderly patients. The potentials of cVEMPs and oVEMPs did not differ significantly between the conventional method and simultaneous recording with monaural stimulation in both the HP and patient groups except the higher amplitude of oVEMPs during the simultaneous recording in both groups. However, during the bilateral simultaneous recording of each VEMP during binaural stimulation, the amplitudes of cVEMPs were reduced in both the HP and patient groups, and the thresholds of cVEMPs increased significantly (tables 1 and 2 and figure 2). From a clinical perspective, these results are encouraging for the use of simultaneous VEMP recording in the clinical routine; they can improve the clinical feasibility of VEMP recording in various vestibular disorders. However, unilateral simultaneous recording of cVEMPs and oVEMPs on each side may be more advocated than the bilateral simultaneous recording because the former uses monaural stimulation, has a more stable physiologic basis, and generates results more compatible to those from the separate recordings in both groups. Furthermore, lower thresholds and higher amplitudes during simultaneous recording with monaural stimulation indicate a better signal-to-noise level with the same loudness. For simultaneous recording of cVEMPs and oVEMPs on each side with monaural stimulation (figure 1A), the only additional request was to look upward compared to the conventional cVEMP recording. Thus, this simultaneous recording method for VEMPs can effectively reduce the time for the recording without causing more difficulties for patients with various vestibular disorders and is a reliable alternative to conventional separate recordings.

Meanwhile, a significant increase in the peak-to-peak amplitude of oVEMP in both groups was demonstrated during simultaneous recording with monaural stimulation, i.e., the oVEMP recorded from the lower eye to ACS stimulation of the upper ear. There have been reports that the oVEMPs to ACS are not affected by head positions.[23–25] One study described no significant differences in oVEMP responses during an upward gaze between the sitting and supine positions, but closing the eyes led to significantly lower amplitude, prolonged latency, and higher threshold.[23] These findings suggest that oVEMP responses are augmented by activation of the inferior oblique ocular muscle rather than head position.[26,27] Another study showed that head tilts in the roll plane significantly increased the amplitude of oVEMPs to bone-conducted vibration recorded from the lower eye compared to those recorded from the upper eye, but the

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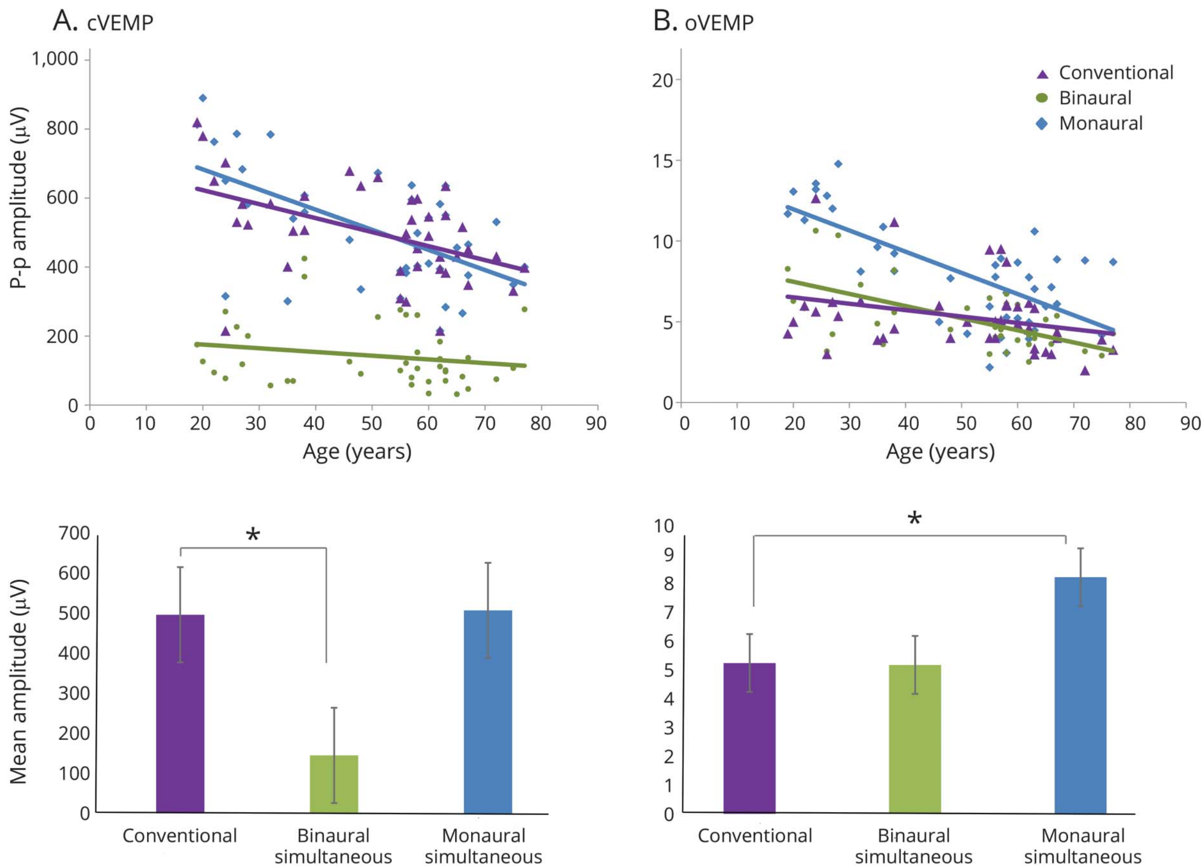
Figure 3 Comparison of cVEMP and oVEMP amplitudes in healthy participants during conventional and simultaneous recording methods



The peak-to-peak (p-p) amplitudes of (A) cervical vestibular-evoked myogenic potentials (cVEMPs) and (B) ocular VEMPs (oVEMPs) plotted as a function of age (top). It revealed a significant correlation between age and the amplitudes of both VEMPs. During the bilateral simultaneous recordings, mean amplitudes of the cVEMPs were significantly lower compared to the conventional separate recordings ($p < 0.001$, paired t test), while the amplitude during monaural stimulation did not differ compared to conventional recordings (A, bottom). The amplitudes of ocular VEMPs (oVEMPs) during monaural stimulation were larger than those from the conventional recordings, while there were no significant differences in oVEMP amplitudes during the bilateral simultaneous recordings (B, bottom) (*$p < 0.05$, bars show SEM).

amplitude of the oVEMPs to ACS did not differ.[25] Therefore, in the head-tilted position and likewise in the current study with head turning and elevation, bone-conducted vibration– or ACS-induced utricular activation may be modulated with the gravitational shear force changes in cases with healthy otoliths.[28,29]

On the other hand, the findings of a significantly higher threshold and reduced amplitude during simultaneous cVEMP recordings with binaural stimulation in both HPs and patients with VN may indicate that bilateral stimulation induces stimulation collision and can affect response strength. However, these findings were not observed during bilateral recordings of oVEMPs. Considering the neural connections of the otoliths, saccular activation evokes inhibitory potentials in the ipsilateral sternocleidomastoid, while in contrast, utricular activation induces ipsilateral inhibitory and contralateral excitatory potentials.[30] Although the utricular input to the ipsilateral cVEMP responses has been considered to be trivial, the utricular contribution to the contralateral excitatory potentials during bilateral recordings of cVEMP with binaural stimulation is unknown. In response to monaural sound stimulation, the contralateral cVEMP, which may be due to utricular activation, manifests as a small, inverted, and slightly delayed peak compared to the ipsilateral cVEMP. Therefore, it is possible that the decreased amplitude of the ipsilateral cVEMP during the simultaneous bilateral recording is caused by contamination from "crossover" utricular excitatory effect on the contralateral sternocleidomastoid.[30] In patients with VN whose utricular function must be decreased, reduction of cVEMP amplitude in the affected side was smaller than in the other side. Otherwise, the neural mechanisms that increase otolith receptor sensitivity with "commissural inhibition" and "cross-striolar inhibition" could affect the results of bilateral recording of the VEMPs. Commissural inhibition and cross-striolar inhibition intensify the sensitivity by combining the inputs from bilateral otolith receptors and the inputs from both sides of the receptors across the striola in a single otolith sensor, respectively.[30] These

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Table 2 Comparison of parameters of VEMPs of patients with VN during unilateral simultaneous cVEMP and oVEMP recordings on each side and bilateral simultaneous recordings of each VEMP vs conventional separate recordings

	n10 Latency, mean ± SD, ms			Amplitude, mean ± SD, μV				
oVEMPs	**Affected**	**Unaffected**	***p* Value[b]**	**Affected**	**Unaffected**	***p* Value[b]**	**AR, %**	**Total test time, min[c]**
Conventional recording	11.9 ± 1.3	11.0 ± 0.7	0.04	2.4 ± 2.1	4.1 ± 2.0	0.02	34.7 ± 36.4	14.9 ± 1.8
Monaural simultaneous	12.1 ± 1.5	11.2 ± 0.9	0.01	2.7 ± 2.0	6.4 ± 2.6	0.01	31.5 ± 31.8	9.3 ± 0.9[d] (62.4%)[e]
***p* Value[a]**	0.84	0.55		0.49	0.03		0.66	<0.001
Binaural simultaneous	11.8 ± 1.3	11.2 ± 0.7	0.59	2.5 ± 1.8	3.8 ± 2.0	0.02	28.4 ± 36.2	7.6 ± 1.2 (51%)[e]
***p* Value[a]**	0.51	0.48		0.80	0.54		0.38	<0.001

	p13 Latency, mean ± SD, ms			Amplitude, mean ± SD, μV				
cVEMPs	**Affected**	**Unaffected**	***p* Value[b]**	**Affected**	**Unaffected**	***p* Value[b]**	**AR, %**	**Total test time, min[c]**
Conventional recording	15.3 ± 1.5	14.1 ± 0.4	0.05	156.3 ± 102.4	235.9 ± 106.5	0.05	21.0 ± 26.2	19.0 ± 1.9
Monaural simultaneous	15.2 ± 1.4	14.3 ± 0.5	0.05	134.1 ± 80.5	233.3 ± 101.0	0.003	33.1 ± 31.4	9.3 ± 0.9[d] (62.4%)[e]
***p* Value[a]**	0.56	0.38		0.55	0.81		0.22	<0.001
Binaural simultaneous	15.1 ± 1.5	14.1 ± 0.9	0.13	57.0 ± 24.6	90.9 ± 36.2	0.03	22.0 ± 33.7	10.3 ± 1.2 (54.2%)[e]
***p* Value[a]**	0.32	0.97		0.001	0.001		0.93	<0.001

Abbreviations: AR = asymmetry ratio; cVEMPs = cervical vestibular-evoked myogenic potentials; oVEMPs = ocular vestibular-evoked myogenic potentials; VN = vestibular neuritis.
p Values by paired *t* test or Wilcoxon signed-rank test for trends as appropriate.
[a] *p* Value compared to conventional sequential recordings.
[b] *p* Value comparing affected and unaffected sides.
[c] The mean required time for VEMPs on both sides excluding the time for preparation, attaching the electrodes, and the threshold test.
[d] Required test time for cVEMPs and oVEMPs on 1 side.
[e] Compared to the conventional sequential recordings, shortened percent of the test time during simultaneous recordings.

mechanisms to increase reactivity to linear acceleration are not effective during bilateral simultaneous stimulation and cause decreased amplitude and increased threshold of the cVEMPs. The stapedial reflex, which is normally observed at >85-dB sound pressure level in humans, could have reduced the amplitudes and increased the thresholds of cVEMPs during bilateral sound stimulation. However, these explanations are inconsistent with the findings of no changes in oVEMP responses, including the peak-to-peak amplitude and thresholds, during bilateral simultaneous recording. Under monaural sound stimulation, ≈25% of normal subjects exhibited ipsilateral negative-positive oVEMP responses,[31] which represents the sum of the crossed effect and may originate from the saccule during bilateral stimulation. Although bilateral simultaneous recordings of oVEMP with binaural stimulation yield the same results as in the monaural conventional recording, we could not exclude the effects of ipsilateral responses, which may occur even during unilateral stimulation.[31] Another possibility for the reduced amplitude and higher threshold of cVEMPs during bilateral recording is the issue of muscle contraction on cVEMP amplitude, which is linear for most of the range of muscle contractions.[32,33]

Author contributions

S.-Y. Oh: conception and design of the study, acquisition and analysis of data, and writing a significant portion of the manuscript or figures. H.-J. Shin, R. Boegle, M. Ertl, and P. zu Eulenburg: acquisition and analysis of data and drafting a significant portion of the manuscript or figures. J.-S. Kim: writing a significant portion of the manuscript and figures. M. Dieterich: conception and design of the study and writing a significant portion of the manuscript and figures.

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Disclosure

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disclosures relevant to the manuscript. R. Boegle is supported by the Graduate School of Systemic Neuroscience and the German Federal Ministry of Education and Research (BMBF grant 01EO140). M. Ertl is supported by the German Federal Ministry of Education and Research (BMBF grant 01EO140) and the German Neurological Foundation. P. zu Eulenburg is supported by the Graduate School of Systemic Neuroscience and the German Federal Ministry of Education and Research (BMBF grant 01EO140). J. Kim reports no disclosures relevant to the manuscript. M. Dieterich is supported by the Graduate School of Systemic Neuroscience, the German Federal Ministry of Education and Research (BMBF grant 01EO140), and the German Neurological Foundation. Go to Neurology.org for full disclosures.

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References

1. Colebatch JG, Halmagyi GM. Vestibular evoked-potentials in human neck muscles before and after unilateral vestibular deafferentation. Neurology 1992;42:1635–1636.
2. Curthoys IS. A critical review of the neurophysiological evidence underlying clinical vestibular testing using sound, vibration and galvanic stimuli. Clin Neurophysiol 2010;121:132–144.
3. Gresty MA, Bronstein AM, Brandt T, Dieterich M. Neurology of otolith function—peripheral and central disorders. Brain 1992;115:647–673.
4. Oh SY, Kim HJ, Kim JS. Vestibular-evoked myogenic potentials in central vestibular disorders. J Neurol 2016;263:210–220.
5. Colebatch JG, Halmagyi GM, Skuse NF. Myogenic potentials generated by a click-evoked vestibulocollic reflex. J Neurol Neurosurg Psychiatry 1994;57:190–197.
6. Todd NPM, Rosengren SM, Aw ST, Colebatch JG. Ocular vestibular evoked myogenic potentials (OVEMPs) produced by air- and bone-conducted sound. Clin Neurophysiol 2007;118:381–390.
7. Oh SY, Kim JS, Lee JM, et al. Ocular vestibular evoked myogenic potentials induced by air-conducted sound in patients with acute brainstem lesions. Clin Neurophysiol 2013;124:770–778.
8. Curthoys IS, Kim J, McPhedran SK, Camp AJ. Bone conducted vibration selectively activates irregular primary otolithic vestibular neurons in the guinea pig. Exp Brain Res 2006;175:256–267.
9. Iwasaki S, Smulders YE, Burgess AM, et al. Ocular vestibular evoked myogenic potentials to bone conducted vibration of the midline forehead at Fz in healthy subjects. Clin Neurophysiol 2008;119:2135–2147.
10. Iwasaki S, McGarvie LA, Halmagyi GM, et al. Head taps evoke a crossed vestibulo-ocular reflex. Neurology 2007;68:1227–1229.
11. Rosengren SM, Welgampola MS, Colebatch JG. Vestibular evoked myogenic potentials: past, present and future. Clin Neurophysiol 2010;121:636–651.
12. Wang SJ, Young YH. Vestibular evoked myogenic potentials using simultaneous binaural acoustic stimulation. Hearing Res 2003;185:43–48.
13. Murofushi T, Takai Y, Iwasaki S, Matsuzaki M. VEMP recording by binaural simultaneous stimulation in subjects with vestibulo-cochlear disorders. Eur Arch Otorhinolaryngol 2005;262:864–867.
14. Ertl M, Boegle R, Kirsch V, Dieterich M. On the impact of examiners on latencies and amplitudes in cervical and ocular vestibular-evoked myogenic potentials evaluated over a large sample (N=1,038). Eur Arch Otorhinolaryngol 2016;273:317–323.
15. Brown MC, Kujawa SG, Liberman MC. Single olivocochlear neurons in the guinea pig, II: response plasticity due to noise conditioning. J Neurophysiol 1998;79:3088–3097.
16. Shin BS, Oh SY, Kim JS, et al. Cervical and ocular vestibular-evoked myogenic potentials in acute vestibular neuritis. Clin Neurophysiol 2012;123:369–375.
17. Oh SY, Kim JS, Yang TH, Shin BS, Jeong SK. Cervical and ocular vestibular-evoked myogenic potentials in vestibular neuritis: comparison between air- and bone-conducted stimulation. J Neurol 2013;260:2102–2109.
18. Papathanasiou ES, Murofushi T, Akin FW, Colebatch JG. International guidelines for the clinical application of cervical vestibular evoked myogenic potentials: an expert consensus report. Clin Neurophysiol 2014;125:658–666.
19. Propst EJ, Greinwald JH, Schmithorst V. Neuroanatomic differences in children with unilateral sensorineural hearing loss detected using functional magnetic resonance imaging. Arch Otolaryngol 2010;136:22–26.
20. Ohwatari R, Fukuda S, Chida E, et al. Preserved otoacoustic emission in a child with a profound unilateral sensorineural hearing loss. Auris Nasus Larynx 2001;28:S117–S120.
21. Krause E, Mayerhofer A, Gürkov R, et al. Effects of acoustic stimuli used for vestibular evoked myogenic potential studies on the cochlear function. Otol Neurotol 2013;34:1186–1192.
22. Colebatch JG, Rosengren SM. Safe levels of acoustic stimulation: comment on "Effects of Acoustic Stimuli Used for Vestibular Evoked Myogenic Potential Studies on the Cochlear Function." Otol Neurotol 2014;35:932–933.
23. Todai JK, Congdon SL, Sangi-Haghpeykar H, Cohen HS. Ocular vestibular evoked myogenic potentials in response to three test positions and two frequencies. Laryngoscope 2014;124:E237–E240.
24. Ito K, Karino S, Murofushi T. Effect of head position on vestibular evoked myogenic potentials with toneburst stimuli. Acta Otolaryngol 2007;127:57–61.
25. Iwasaki S, Chihara Y, Egami N, Fujimoto C, Murofushi T, Yamasoba T. Different effects of head tilt on ocular vestibular-evoked myogenic potentials in response to bone-conducted vibration and air-conducted sound. Exp Brain Res 2012;223:389–396.
26. Rosengren SM, McAngus Todd NP, Colebatch JG. Vestibular-evoked extraocular potentials produced by stimulation with bone-conducted sound. Clin Neurophysiol 2005;116:1938–1948.
27. Govender S, Rosengren SM, Colebatch JG. The effect of gaze direction on the ocular vestibular evoked myogenic potential produced by air-conducted sound. Clin Neurophysiol 2009;120:1386–1391.
28. Dai MJ, Curthoys IS, Halmagyi GM. Linear acceleration perception in the roll plane before and after unilateral vestibular neurectomy. Exp Brain Res 1989;77:315–328.
29. Taylor RL, Xing MZ, Black DA, Halmagyi GM, Welgampola MS. Ocular vestibular evoked myogenic potentials: the effect of head and body tilt in the roll plane. Clin Neurophysiol 2014;125:627–634.
30. Uchino Y, Kushiro K. Differences between otolith- and semicircular canal-activated neural circuitry in the vestibular system. Neurosci Res 2011;71:315–327.
31. Wang SJ, Jaw FS, Young YH. Ocular vestibular-evoked myogenic potentials elicited from monaural versus binaural acoustic stimulations. Clin Neurophysiol 2009;120:420–423.
32. Bess FH, Tharpe AM. An introduction to unilateral sensorineural hearing-loss in children. Ear Hearing 1986;7:3–13.
33. Bess FH. Special issue: unilateral sensorineural hearing-loss in children: foreword. Ear Hearing 1986;7:2.

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Simultaneous recording of cervical and ocular vestibular-evoked myogenic potentials

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Trial registration number: NCT03049683.

Study question

Can simultaneous recordings of ocular and cervical vestibular-evoked myogenic potentials (VEMPs) reduce recording times without compromising the diagnostic utility of VEMP-based otolithic function evaluations relative to that achieved with sequential recordings?

Summary answer

Simultaneous recordings reduce recording times without compromising utility.

What is known and what this paper adds

Cervical and ocular VEMP recordings are useful for assessing otolithic function, but sequential recordings are time-consuming. This study provides evidence that simultaneous recordings reduce recording times without compromising diagnostic utility.

Design

This study involved a systematic crossover head-to-head comparison of (1) unilateral simultaneous ocular and cervical VEMP recordings during monaural stimulation, (2) bilateral simultaneous ocular or cervical VEMP recordings during binaural stimulation, and (3) sequential recordings. Each participant underwent all protocols in random order. The protocols were performed on different days at 1- or 2-day intervals. The study was nonblinded.

Participants and setting

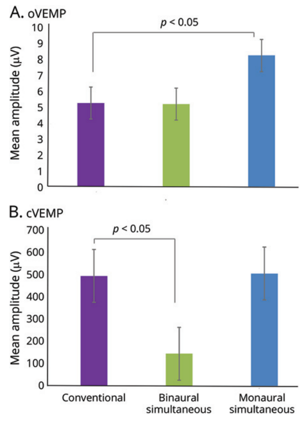
The study included adult healthy participants (HPs) and patients with acute vestibular neuritis. This single-center study was conducted in March to August 2016.

Primary outcome(s)

The primary outcomes were the total recording times and VEMP parameters for the simultaneous and sequential protocols.

Main results and the role of chance

Relative to the sequential protocol, recording times were significantly reduced with the unilateral simultaneous (by 48% for HPs, by 62.4% for patients) and bilateral simultaneous (by 56.5% for HPs, by 52.6% for patients) protocols ($p < 0.001$ for all). The unilateral simultaneous protocol had little effect on VEMP thresholds and latencies but increased ocular VEMP amplitudes ($p \leq 0.04$ in HPs, $p = 0.03$ in patients on the unaffected side). The bilateral simultaneous protocol reduced cervical VEMP amplitudes in both groups ($p < 0.001$ in HPs, $p = 0.001$ in patients). However, the observed changes with simultaneous protocols would not reduce the diagnostic utility of the VEMP recordings.



Harms

Sound intensities during VEMP recordings may damage hearing, so reduced recording times are desirable.

Bias, confounding, and other reasons for caution

Various reflexes and potential nerve activations may have contaminated the results.

Generalizability to other populations

The HPs' mean age (33.1 years) was much lower than the patients' mean age (63.5 years). VEMP amplitudes and thresholds are age dependent, so each group's results may not be generalizable to persons of different ages.

Study funding/potential competing interests

The research was funded by universities, government agencies, and medical research foundations. There are no competing interests. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The authors of the full-length article and the journal editors edited and approved the final version.

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