Practice guideline: Cervical and ocular vestibular evoked myogenic potential testing

ABSTRACT
Objective: To systematically review the evidence and make recommendations with regard to diagnostic utility of cervical and ocular vestibular evoked myogenic potentials (cVEMP and oVEMP, respectively). Four questions were asked: Does cVEMP accurately identify superior canal dehiscence syndrome (SCDS)? Does oVEMP accurately identify SCDS? For suspected vestibular symptoms, does cVEMP/oVEMP accurately identify vestibular dysfunction related to the saccule/utricle? For vestibular symptoms, does cVEMP/oVEMP accurately and substantively aid diagnosis of any specific vestibular disorder besides SCDS?

Methods: The guideline panel identified and classified relevant published studies (January 1980–December 2016) according to the 2004 American Academy of Neurology process.

Results and Recommendations: Level C positive: Clinicians may use cVEMP stimulus threshold values to distinguish SCDS from controls (2 Class III studies) [sensitivity 86%–91%, specificity 90%–96%]. Corrected cVEMP amplitude may be used to distinguish SCDS from controls (2 Class III studies) [sensitivity 100%, specificity 93%]. Clinicians may use oVEMP amplitude to distinguish SCDS from normal controls [3 Class III studies] [sensitivity 77%–100%, specificity 98%–100%]. cVEMP threshold may be used to aid in distinguishing SCDS from controls (3 Class III studies) [sensitivity 70%–100%, specificity 77%–100%]. Level U: Evidence is insufficient to determine whether cVEMP and oVEMP can accurately identify vestibular function specifically related to the saccule/utricle, or whether cVEMP or oVEMP is useful in diagnosing vestibular neuritis or Ménière disease. Level C negative: It has not been demonstrated that cVEMP substantively aids in diagnosing benign paroxysmal positional vertigo, or that cVEMP or oVEMP aids in diagnosing/managing vestibular migraine. Neurology® 2017;89:2288-2296

GLOSSARY
AAN = American Academy of Neurology; BPPV = benign paroxysmal positional vertigo; CI = confidence interval; cVEMP = cervical vestibular evoked myogenic potential; nHL = normal hearing level; oVEMP = ocular vestibular evoked myogenic potential; SCDS = superior canal dehiscence syndrome; VEMP = vestibular evoked myogenic potential; VM = vestibular migraine; VN = vestibular neuritis.

Types of VEMP testing. There are 2 types of VEMP testing: cervical VEMP (cVEMP) and ocular VEMP (oVEMP).

- The cVEMP test is believed to assess saccular vestibular signals carried via the vestibulospinal tract. cVEMP is performed by applying sound stimulation to 1 ear while recording surface EMG over the ipsilateral sternocleidomastoid muscle (figure 1). Sound-responsive vestibular cells, mainly within the inner ear saccule, momentarily inhibit ipsilateral muscle tone...
via the cervical vestibulocollic pathway (figure 2).8–10 Surface EMG responses from the tonically contracted ipsilateral sternocleidomastoid muscle are averaged to yield a biphasic waveform response (figure 3). cVEMP responses can also be derived from the mas- seter, triceps, and gastrocnemius muscles.11,12 The oVEMP test is believed to measure vestibular function from the utricle via the superior vestibular nerve, which then crosses the midline to the contra- lateral medial longitudinal fasciculus and the oculo- motor nucleus (figure 4).9,13 oVEMP does not substantially involve the semicircular canals.14 oVEMP uses an air- or bone-conducted sound stimulus and averages the surface EMG responses from the contralateral inferior oblique muscle (figure 4) to yield a biphasic waveform (figure 5). Measurements are made of the latencies of the early peaks (n10 or n1 and p16 or p2 for oVEMP) and a peak-to-peak amplitude (figure 5).

Technical considerations in VEMP. cVEMP technical standards have been proposed.15 VEMP responses attenuate after age 60 years, and thus the studies included here apply to people aged < 60 years.16,17 Sensorineural hearing loss does not affect cVEMP/ oVEMP.18 Conductive hearing loss may reduce sound intensity at the oval window and render VEMP responses unobtainable. For both cVEMP and oVEMP, the minimum sound stimulus needed to evoke a biphasic VEMP response is called the threshold (table e-1 at Neurology.org).

This guideline addresses published evidence related to cVEMP and oVEMP for peripheral vestibular disorders.

Superior canal dehiscence syndrome. Superior canal dehiscence syndrome (SCDS) is caused by an abnormal opening (dehiscence) in the temporal bone that forms the roof of the superior semicircular canal.19 Overall, 1%–2% of the population has abnormal thinning of the temporal bone near the superior semicircular canal.20 Further erosion may occur with age.21 The average age at diagnosis is 46 years.22 Dehiscence renders the membranous labyrinth unusually susceptible to sound and pressure changes.

SCDS diagnosis is based on the combination of vestibular and auditory signs and symptoms and tem- poral bone CT. Patients with SCDS commonly report pressure-induced (coughing, sneezing, straining) and sound-induced vertigo, dizziness, and the Tullio phenomenon (dizziness induced by sound) or autophony (hearing one’s internal body sounds) due to increased sensitivity to sound conducted through bone. Clinical examination may reveal eye movements induced by Valsalva maneuvers, by pres- sure in the external auditory canal, or by sounds.19,23 Patients may have an air–bone gap, especially at the lower frequencies.24 For those with disabling symp- toms, case series suggest a benefit with surgical plug- ging or resurfacing of the bony opening.25

A 2000 American Academy of Neurology (AAN) guideline provides guidance on vestibular testing techniques in adults and children.26 In this new guideline, 4 questions were asked regarding the diagnostic accuracy of cVEMP and oVEMP: (1) Does cVEMP accurately identify SCDS? (2) Does oVEMP accurately identify SCDS? (3) For suspected vestibular symptoms, does cVEMP/oVEMP accurately identify vestibular dysfunction related to the saccule/ utricle? (4) For vestibular symptoms, does cVEMP/ oVEMP accurately and substantively aid in diagnosis of any specific vestibular disorder besides SCDS?

DESCRIPTION OF THE ANALYTIC PROCESS
In September 2010, the AAN guideline subcommittee convened an expert panel to develop this practice guideline (appendices e-1 and e-2), following the pro- cess described in the 2004 AAN process manual.27 The panel searched MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL), Literatura Latino Americana em Ciências da Saúde (LILACS), and Science Citation Index for relevant articles in all languages published from January 1, 1980, through March 1, 2015, finding only relevant articles in...
Analyses of Evidence

Does cVEMP Accurately Identify Patients with SCDS?

There were 9 Class III studies. A meta-analysis was considered but not performed given the heterogeneity of the studies.

**cVEMP threshold.** There were 2 positive Class III studies and another Class III study downgraded for the question of threshold due to incorporation bias. The first study was a retrospective cohort of 65 patients. At the 500-Hz tone bursts, VEMP thresholds were 66 dB (95% confidence interval [CI] 62.1–67.0 dB) for SCDS ears and 85 dB (95% CI 82.6–87.4 dB) for non-SCDS ears. The cVEMP using a threshold of ≤65 dB normal hearing level (nHL) yielded 91.4% sensitivity and 95.8% specificity.

The second study (case control) examined the cVEMP threshold values of 29 patients with suspected SCDS and 50 healthy control ears. The best combination of sensitivity and specificity was found using cVEMP threshold of ≤85 dB nHL, which yielded 86% sensitivity (95% CI 66%–95%) and 90% specificity (95% CI 77%–96%) in separating patients with SCDS from controls.

**cVEMP amplitude.** Two negative underpowered Class III studies showed that cVEMP raw amplitude possibly did not effectively detect SCDS. The first study of 67 patients compared 17 CT-demonstrated SCDS ears with 107 CT-demonstrated non-SCDS ears. After a Bonferroni correction, no significant differences were found. The second study used a striker to enhance cVEMP responses and included 5 patients with SCDS and 20 normal controls. The mean amplitudes were 53.3 µV (95% CI 29.9–76.8 µV) for controls and 63.1 µV (95% CI 52.0–74.4 µV) for those with SCDS, but there was too much overlap to separate SCDS ears from controls.

**Corrected cVEMP amplitude.** There were 5 Class III studies that addressed corrected VEMP amplitudes. For air-conducted cVEMP amplitudes, lower stimulus intensity may be more effective.
at distinguishing SCDS from normal because of saturation at greater stimulus intensities.28,32
The first study examined 20 healthy controls vs SCDS ears in 10 affected patients29 and found the VEMP-corrected amplitude of SCDS-affected ears, 2.78 (95% CI 2.69–2.87), was significantly greater than in controls, 1.29 (95% CI 1.22–1.37). The study also found surgical repair of the dehiscence with canal plugging resulted in normalization of corrected cVEMP amplitudes.

The second study reported a mean corrected amplitude of 0.23 ± 0.28 (95% CI 0.18–0.28) for 113 controls and 1.75 ± 0.61 (95% CI 1.50–2.01) for 22 SCDS ears.32 With use of a corrected cVEMP amplitude of 0.8 (determined from normal mean 0.23 + 2 SD), cVEMP amplitude had a sensitivity of 100% (22/22) and specificity of 93% (115/113).

In the third study, patients with SCDS had a significantly larger mean corrected amplitude, 3.0 (95% CI 2.41–3.56), than controls, 1.25 (95% CI 1.05–1.45).34 Of patients and controls aged >40 years, 93.8% had corrected amplitude values greater than the mean +2 SD of the control group. However, neither the sensitivity nor the specificity could be determined in this subset.

The fourth study (underpowered) compared 11 patients who had SCDS with 11 controls.29 The mean difference between the corrected peak-to-peak amplitudes for patients with SCDS and controls was not significant for click stimulus, 2.2 (95% CI 0.1–4.3), or tone burst stimulus, 3.5 (95% CI 0–7.1).

The final study compared 13 patients who had known SCDS with 15 normal controls.28 With use of a stimulus intensity of 105 dB pSPL and a corrected amplitude cutoff of 2.5 SD above the controls mean, cVEMP had a sensitivity of 100% (13/13) and specificity of 93% (14/15) in distinguishing patients with SCDS from controls.

Conclusions. cVEMP threshold values possibly distinguish patients with SCDS from controls (2 Class III studies) with sensitivity of 86%–91% and specificity of 90%–96%. Corrected cVEMP amplitude possibly distinguishes patients with SCDS from controls (2 Class III and 3 underpowered Class III studies) with sensitivity of 100% and specificity of 93%. Raw cVEMP amplitude possibly do not distinguish patients with SCDS from controls (2 underpowered Class III studies).

Recommendations. Clinicians may use cVEMP threshold values to distinguish patients with SCDS from controls (Level C). Corrected cVEMP amplitude may also be used to distinguish patients with SCDS from controls (Level C).

Does oVEMP accurately identify patients with SCDS? Seven Class III studies were identified.25,28,29,31,35–37
oVEMP amplitude. One retrospective study looked at 9 patients with SCDS matched to controls.35 Mean raw amplitudes were greater in SCDS ears, 2.68 μV (95% CI 2.46–2.90 μV), than in controls, 0.93 μV (95% CI 0.91–0.95 μV). Using an n10 amplitude of ≥1.5 μV, oVEMP had 100% sensitivity and 100% specificity in differentiating patients with SCDS from controls.

A second study28 compared SCDS ears with normal ears. The mean amplitude of patients with SCDS was significantly higher, 35.9 μV (95% CI 26.7–45.1 μV), than controls, 8.9 μV (95% CI 6.24–11.56 μV). With use of a stimulus intensity of 105 dB pSPL and corrected amplitude of ≥2.5 SD above the mean of normal controls, oVEMP amplitudes had a 77% (10/13) sensitivity and 100% (15/15) specificity in distinguishing SCDS ears from normal ears.

A third study examined the oVEMP n10 amplitude of 29 ears in patients with suspected SCDS compared with 50 control ears.25 Use of an n10 amplitude of ≥9.3 μV as the cutoff yielded a sensitivity of 100% (95% CI 88%–100%) and specificity of 100% (95% CI 93%–100%). Using an oVEMP peak-to-peak amplitude of >17.1 μV as the cutoff resulted in 100% sensitivity (95% CI 85%–100%) and 98% specificity (95% CI 89%–100%).

A fourth study, described previously, compared oVEMP n10 amplitudes using 4 different stimuli.29 Use of an n10 amplitude of ≥8.25 μV as the cutoff yielded a sensitivity of 100% (95% CI 72%–100%) and a specificity of 100% (95% CI 72%–100%).

In a fifth study comparing SCDS ears with normal ears,31 controls had a mean of 12.31 μV (95% CI 10.9–13.7 μV), SCDS-affected ears had a mean of 4.3 mice.28,29,31,35–37

The recordings are from the right sternocleidomastoid muscle in response to 500-Hz tone bursts (2 ms duration, 2 ms rise/fall), with an intensity of 130 dB pSPL. The waveform shows the positive-negative cVEMP (p13-n23) on the side to which the sound stimulation is applied. Measurements include the latency, the amplitude, and the threshold (least intense sound stimulus to still yield a reliable response). The responses occur only on the side of the sound stimulation. Some laboratories display an inverted waveform with the positive wave up instead of the negative wave up. © Barrow Neurological Institute, Phoenix, AZ. Used with permission.
12.14 μV, but no information was given about SDs, and sensitivity and specificity could not be determined.

**oVEMP evoked by stimulus 4,000-Hz tone burst at the midline forehead.** One study, aiming to find a single method to distinguish SCDS ears from normal ears, compared 30 SCDS ears with 44 control ears after application of a 4,000-Hz sound stimulus to the midline forehead. All SCDS ears had an oVEMP response, and none of the 44 healthy ears had an oVEMP response, yielding 100% sensitivity and 100% specificity.

**oVEMP threshold.** Two studies supported use of oVEMP stimulus threshold.28,37

The first study, comparing 10 SCDS ears with those of 10 normal controls, found that the mean threshold in patients with SCDS was 101.2 ± 5.5 dB pSPL compared with 116.7 ± 4.7 dB pSPL for controls (p < 0.001), and all patients with SCDS had abnormally low threshold values.37

The second study, described earlier, found that using an oVEMP stimulus threshold value <105 dB pSPL achieved a sensitivity of 100% (13/13) and specificity of 92% (14/15). When a threshold of <99 dB pSPL as abnormal was applied, patients with SCDS were differentiated from controls with sensitivity of 76.9% (10/13) and specificity of 93.3% (14/15).28

**Conclusions.** oVEMP amplitude possibly distinguishes SCDS from normal controls (3 Class III, 2 underpowered or inconclusive studies) with a sensitivity range of 77%–100% and a specificity range of 98%–100%. The efficacy is unknown for use of a 4,000-Hz stimulus to determine the presence or absence of an oVEMP response to differentiate ears with SCDS from normal ears (1 positive Class III study). An oVEMP threshold below a laboratory-specific value (usually 2 SD below the mean threshold of controls) possibly distinguishes SCDS ears from normal ears with a sensitivity of 77% and a specificity of 93% (2 Class III studies).

**Recommendation.** oVEMP testing using either specific thresholds or amplitudes may be used in patients to aid in making an SCDS diagnosis (Level C).
Clinical context for VEMP testing for SCDS. Both cVEMP and oVEMP in SCDS may show an abnormal response that is actually hyperactive. That is, SCDS requires a less intense sound stimulus than normal (i.e., lower threshold) to induce the response, and the response amplitude is abnormally increased on the affected side. No other vestibular disorder has yet demonstrated hyperactive VEMP responses to such a degree.

The false appearance of dehiscence by CT of the temporal bone can sometimes be seen in patients without SCDS. In some cases, a negative CT of the temporal bone but abnormal VEMP is due to dehiscence in a canal other than the superior canal. To confirm SCDS, cVEMP and oVEMP provide a physiologic correlate to the clinical symptoms and the temporal bone CT findings. Hence, VEMP studies serve a complementary role in conjunction with temporal bone CT and clinical history in SCDS diagnosis. Normalization of VEMP amplitudes and thresholds after successful surgical repair of SCDS is further confirmation that VEMP studies correlate with the presence of a physiologically significant degree of dehiscence.

For patients with suspected vestibular symptoms, does cVEMP/oVEMP accurately identify vestibular dysfunction related to the saccule/utricle? Because there is no reference standard test for isolated saccular/utricular loss, no method exists to directly determine in humans whether cVEMP responses reflect saccular function and whether oVEMP responses reflect utricular function. The guideline authors found studies correlating caloric vestibular loss with absence of oVEMP responses in vestibular neuritis (VN), but this only implies the relationship. Ultimately, this question was unanswerable using AAN guideline methodology.

Clinical context for VEMP as a measure of saccular dysfunction and oVEMP as a measure of utricular dysfunction. Historically, animal studies have been essential in understanding the vestibular system. For example, animal studies were a critical part of determining that caloric testing is a measure of horizontal semicircular canal function, which is now accepted. In the case of VEMP, animal studies suggest that cVEMP is most closely tied to function of the saccule and oVEMP to the utricle, although with some possible contribution from the semicircular canals.

Conclusion. It is not known whether oVEMP/ cVEMP responses accurately identify vestibular function specifically related to the saccule/utricle (no relevant studies).

Recommendation. cVEMP and oVEMP have unknown efficacy in accurately identifying vestibular function specifically related to the saccule/utricle (Level U).

For patients with vestibular symptoms, does cVEMP/ oVEMP accurately and substantively aid diagnosis of any specific vestibular disorder besides SCDS? Vestibular neuritis. Class III studies have applied VEMP to VN. VEMP is viewed as helpful in identifying whether VN has led to dysfunction related to the superior or inferior (or both) branches of the vestibular nerve supporting rather than making the diagnosis.

Clinical context. VN remains a clinical diagnosis with symptoms of acute vestibular dysfunction, normal hearing, and typical signs. Use of VEMP to parse out which parts of the nerve or labyrinth are affected is predicated on the notion that cVEMP is indicative of saccular function and oVEMP of utricular function. Although this notion is biologically plausible and supported by animal studies, and studies of VN have found that caloric loss correlates strongly with absence of oVEMP responses, direct evidence in humans of the type acceptable within the AAN guideline process is currently absent.

Conclusion. Expert consensus supports use of cVEMP and oVEMP to determine the extent of VN involvement, but with the methods used herein, no such determination can be made.

Recommendation. Evidence is insufficient to determine whether cVEMP/oVEMP use would clarify which vestibular structures are affected in VN (Level U).

Ménière disease. All 8 studies on Ménière disease are Class III, most of which were downgraded because of spectrum bias.

One study examined the ratio of oVEMP amplitudes at 500-Hz and 750-Hz sound stimulus.
Comparing the amplitude ratio of 750 Hz to 500 Hz with cutoff of >1.21 yielded a sensitivity of 89% and a specificity of 100% when patients with Ménière disease were compared with controls.

Another study showed no distinction of Ménière disease from controls for cVEMP/oVEMP.

Other Class III studies also examined cVEMP in Ménière disease. None demonstrated an ability as a stand-alone diagnostic test to reliably diagnose Ménière disease. Some showed vestibular dysfunction manifesting as an ipsilaterally absent response.

Conclusions. On the basis of multiple conflicting or inconclusive studies, neither cVEMP nor oVEMP testing was found to be useful in diagnosing Ménière disease, but the studies possibly demonstrate that vestibular loss as assessed by VEMP may be seen in Ménière disease.

Recommendations. cVEMP may be used as an ancillary test in Ménière disease for vestibular dysfunction (Level C). There is insufficient evidence that either cVEMP or oVEMP may be used to diagnose Ménière disease (Level U).

Clinical context for using VEMP in Ménière disease. The diagnosis of Ménière disease has long been a clinical one, and only recently has audiometry been added as a diagnostic test to reliably diagnose Ménière disease. Some showed vestibular dysfunction manifesting as an ipsilaterally absent response.

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specifically identified; (4) does not mandate any particular course of medical care; and (5) is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient. Use of the information is voluntary. AAN provides this information on an “as is” basis, and makes no warranty, expressed or implied, regarding the information. AAN specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. AAN assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.

CONFLICT OF INTEREST The American Academy of Neurology is committed to producing independent, critical, and truthful practice guidelines. Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this practice guideline. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the practice guidelines and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, a network of neurologists, Neurology peer reviewers, and representatives from related fields. The AAN Guideline Conflict of Interest Policy can be viewed at aan.com. For complete information on this process, access the 2004 AAN process manual.27

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