cVEMPs: A systematic review and meta-analysis

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Abstract

Objective: A systematic literature review and meta-analysis was performed to determine the effect of stimulus type, SCM muscle activation method, transducer type, and method to control SCM muscle EMG level on response parameter values for 0.1-ms click-evoked and 500-Hz tone burst cVEMPs. A description of normative response values was attempted. *Design:* An electronic systematic literature review was performed to obtain normative cVEMP response data. Subsequently a meta-analysis was conducted to determine significant effects on cVEMP response parameters and to obtain norms. *Study sample:* Scopus was used to identify reports containing normative data. Reports were selected based on inclusion and exclusion criteria determined beforehand. Weighted means were calculated and compared to identify significant effects and normative data. *Results:* Sixty-six reports were included in the systematic review. Stimulus type, SCM muscle activation method, transducer type, and method to control SCM muscle EMG level had significant effects on all response parameters. *Conclusions:* Optimal stimulus and recording parameters suggested by previous research are confirmed by the current systematic review and meta-analysis and are suggested for clinical use. Response parameter values are influenced by variations in stimulus and recording parameters and normative response values are suggested as guideline for cVEMP interpretation.

Key Words: Cervical vestibular evoked myogenic potential; normative data

Vestibular function testing commonly consists of a battery of tests. A relatively recent addition to the test battery for evaluating vestibular function is the vestibular evoked myogenic potential (VEMP) (Rosengren et al, 2010).

Although the work of Dr. Pietro Tullio on alert animals paved the way for studying the acoustic sensitivity of the vestibular system, von Békésy (in 1935) was the first to describe sound-evoked vestibular responses in normal human subjects (Welgampola & Colebatch, 2005). More recently, Colebatch and Halmagyi (1992) and Colebatch et al (1994) measured electromyographic (EMG) activity from the sternocleidomastoid (SCM) muscle in response to high-level, air-conduction clicks. This established a reliable procedure to record myogenic potentials evoked by clicks and the cervical or collic 'cVEMP' became a practical, clinical test. The response could be depicted as an initial positive peak (p13 or P1), followed by a successive negative peak (n23 or N1). Although VEMPs are currently also measured over the ocular muscles, the present study will refer to the described cVEMP.

In short, the cVEMP can be described as an inhibitory potential recorded from the SCM muscle due to saccular activation in response to loud sounds (Zhou & Clarke Cox, 2004). When measuring the cVEMP, tonic SCM muscle contraction generates background EMG which is interrupted briefly due to a short period of inhibition (Welgampola & Colebatch, 2005; Rosengren et al, 2010).

The last decade has been marked with studies attempting to identify whether air conduction clicks or tone bursts are best suited for clinical use. It seems that the majority of data indicate short tone bursts to be superior to click stimuli when attempting to evoke cVEMP responses, since they produce larger cVEMP amplitudes, have better reliability across recording sessions, and have smaller inter-laboratory variability (Welgampola & Colebatch, 2001a; Murofushi et al, 1999; Basta et al, 2005; Wu et al, 2007; Viciana & Lopez-Escamez, 2012).

Stimulus parameters have definite effects on cVEMP response parameters, and optimal parameters are suggested by various studies (Zhou & Clarke Cox, 2004; Zapala, 2007; Young, 2006; Wuyts et al, 2007). Some variability concerning recording parameters is also evident across the literature. This includes SCM muscle activation method, electrode montage, transducer type, amplifier gain, filter settings, time window for recording, number of sweeps, and tone burst frequency (Zhou & Clarke Cox, 2004; Cheng & Morufushi, 2001a, 2001b; Welgampola & Colebatch, 2001a). Evidence-based stimulus and recording parameters still need to be suggested.

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Abbreviations

AR	Asymmetry ratio
CV	Click cVEMP
cVEMP	Cervical vestibular evoked myogenic potential
EMG	Electromyographic
MRV	Mean rectified voltage
SCM	Sternocleidomastoid
TBV	Tone burst cVEMP

There are two basic techniques used to activate the SCM muscles during cVEMP testing; one being head rotation and the other neck flexion. Both can be done with the patient either in a sitting or a supine position. The neck flexion method has several variations and SCM muscle activation is achieved by lifting the head against gravity in the supine position or by pushing the head forward against a padded bar whilst in the sitting position (Ozdek et al, 2009; Akin et al, 2004; Welgampola & Colebatch, 2005). Isaacson and colleagues (2006) compared three methods of SCM muscle activation and found that eliciting cVEMPs with the subject in the supine position with the head turned to the contralateral side of stimulation leads to the most robust amplitudes. Wang and Young (2006) compared the head rotation method in the sitting position and the head elevation method with the head in the midline position and found that when combining results of both the head elevation and head rotation methods, a higher response rate was obtained.

The response parameters used to describe and interpret the P1-N1 complex include P1 and N1 latency, P1-N1 amplitude, threshold and asymmetry ratio. Lately, corrected P1-N1 amplitude and threshold values are used more often to interpret cVEMP responses. However, latency is a robust parameter since test-retest reliability has been proven to be good and intra-subject variations are described as being small (Versino et al, 2001; Eleftheriadou & Koudounarakis, 2011).

Raw, unrectified amplitude values vary widely, leading to great inter- and intra-subject variability. There is a general agreement across click and tone burst evoked studies that an increase in intensity will lead to a corresponding increase in response amplitude, under the condition of an equal SCM muscle contraction level throughout all recordings (Wit & Kingma, 2006; Welgampola & Colebatch, 2001a; Colebatch et al, 1994). Stimulus frequency also has a definite effect on cVEMP response amplitude and the saccule exhibits maximum resonance at lower frequencies (Todd et al, 2000; Park et al, 2010). A linear relationship between stimulus duration and cVEMP amplitude is expected where an increase in tone burst plateau and rise and fall time, as well as overall click duration will lead to an increase in response amplitude (Welgampola & Colebatch, 2001a; Cheng & Morufushi, 2001b, 2001a).

Perhaps the leading cause of variability among cVEMP responses is differences in tonic EMG measured over the SCM muscles. It has been well-documented that amplitude scales in proportion to tonic EMG activity (Colebatch et al 1994; Akin et al, 2004; Isaacson et al, 2006). Therefore, monitoring the tonicity of the SCM muscle is a prerequisite for accurate cVEMP recording. Vanspauwen et al (2006) described using a blood pressure manometer for visual feedback as a valid alternative to EMG measurement when simultaneous MRV and cVEMP recording is not feasible.

cVEMP threshold is defined as the lowest stimulus intensity where a clear biphasic response can be elicited and seems to be a useful and reliable parameter (Eleftheriadou & Koudounarakis, 2011). For click-evoked cVEMPs, thresholds have been found to be within 75–85 dB nHL (Colebatch et al, 1994), but Welgampola and Colebatch (2001b) found a threshold range of up to 100 dB nHL to be normal. A normative threshold range across studies has not been established.

Due to large inter-subject variability regarding cVEMP amplitude, clinicians express the side-to-side difference in raw or corrected amplitude as a percentage. This asymmetry ratio (AR) is calculated by the following formula:

$$AR = 100 \times (AL - AS)/(AL + AS),$$

where AL equals the larger P1-N1 amplitude and AS the smaller P1-N1 amplitude. Although Wu et al (2007) found no statistically significant AR differences between click- and tone burst-evoked cVEMPs, the AR is still dependent on amplitude values and substantial variations between ears are evident in even normal subjects (Lee et al, 2008). Several researchers have suggested norms, but they vary widely between studies (Li et al, 1999; Welgampola & Colebatch, 2001a; Maes et al, 2009). Thus, as with latency, amplitude and threshold, normative data are still needed.

Aging has a definite effect on the vestibular system and the changes in cVEMP responses with age have been well-documented. There seems to be a general consensus in the literature that cVEMP responses can be reliably evoked up until the age of 60. Thereafter, if present, cVEMPs should be interpreted with great care in terms of amplitude and threshold (Welgampola & Colebatch, 2001b; Lee et al, 2008; Rosengren et al, 2011; Su et al, 2004).

Eleftheriadou and Koudadounarakis (2011) concluded that there is a lack of consensus on procedures for cVEMP recording and interpretation. Even though several studies across the literature have attempted to describe the best stimulus and recording parameters, relatively small sample sizes were used. In an effort to overcome this problem, a meta-analysis can be performed to compensate for small study groups (Glass, 1976). This pooling of data can lead to more precise estimates and facilitates consistency of evidence across studies. Therefore, this study aimed to determine the most prevalent trends in stimulus and recording parameters by performing a systematic literature review. Also, it aimed to combine normative data to determine significant effects of stimulus type, SCM muscle activation method, transducer type, and method to control SCM muscle EMG level on cVEMP results by performing a meta-analysis and to obtain normative guidelines for cVEMP interpretation.

Method

Systematic review

Relevant current publications in peer-reviewed journals were sourced electronically through a computerized literature search to obtain normative response data. The Scopus database was used to enable a multi-pronged search strategy, seeing that it covers multiple health-related databases and has full Medline and PubMed coverage. The indicator 'VEMP' was entered as search term for all years up until 2012. Reports from 1974–2012 were sourced. Non-English reports, duplicates, reviews, letters, notes, dissertations and conference papers were excluded. Full-text articles were then retrieved for all remaining studies.

Reports were only included if normative control group data were reported and control group participants had to present with normal hearing with no history of vestibular function deficits. Additionally, reports that explicitly aimed to determine normative data were included. Participants had to be between the ages 18 and 60 to exclude possible vestibular function deterioration due to aging. Males and females were included, since there is no clear indication that gender has an effect on cVEMP results (Tourtillott et al, 2010;

Welgampola & Colebatch, 2001b). Only studies where cVEMPs were conducted via air conduction stimuli were included.

After the full-text reports were reviewed to determine whether they meet the inclusion criteria, they were divided into two main groups: those dealing with clicks and those dealing with tone bursts. Each report in these two main groups was then carefully analysed with respect to the following parameters: (1) report title; (2) year of publication; (3) number of participants; (4) mean age of participants; (5) device used for cVEMP testing; (6) SCM muscle activation method (seated, turn head contralaterally *'STC'*; supine, head elevated *'SEH'*; supine, elevate and rotate head contralaterally *'SETC'*; seated, push head forward *'SPF'*; supine, head rotated *'SRH')*; (7) electrode montage; (8) transducer used; (9) method to control SCM muscle EMG level (rectified cVEMPS; visual monitoring only; rectified cVEMPs and visual monitoring; the blood pressure feedback method only; controlling method not indicated); (10) stimulus parameters (stimulus type, frequency, polarity, level, rate, duration, rise and fall time, plateau, gating); (11) recording parameters (amplifier gain, filter settings, time window, number of sweeps, number of channels); and (12) response parameters (mean latency P1, mean latency N1, mean amplitude, mean asymmetry ratio, mean threshold).

Meta-analysis

A meta-analysis was performed to combine cVEMP test results from the individual studies to determine significant effects of stimulus type, SCM muscle activation method, transducer used, and method to control SCM muscle EMG level, as well as normative data for cVEMP interpretation. Thus, all reports from the systematic review indicating normative means for latency, amplitude, asymmetry ratio and threshold were included. Microsoft Excel was used to perform the meta-analysis measures for 0.1-ms click cVEMPs (CVs) and 500-Hz tone burst cVEMPs (TBVs).

Documented means of all response parameters (latency P1, latency N1, raw amplitude, corrected amplitude, asymmetry ratio and threshold), and number of participants in each study were used to calculate weighted means, standard deviations and 95% confidence intervals (CI) for CVs and TBVs. In order to calculate the weighted means, a weight was assigned to each study according to the number of participants in each study ($w_i = \frac{n_i}{N}$, where n_i is the number of participants in study i, and N is the total number of participants across all the studies). The original means were then re-weighted ($X_i = w_i \times x_i$, where x_i is the un-weighted mean of study i). The weighted sample mean of each response parameter was then determined $(E(\bar{X}_j) = \frac{\sum w_i x_i}{\sum w_i}$, where i is the particular study, w_i is the proportion of participants in study i and x_i is the un-weighted mean of study i). The standard deviations for each response parameter was determined by $S_j = \sqrt{(\frac{1}{n-1})\sum (x_i - \bar{x}_j)^2}$, and the 95% CI by $CI_{95\%} = (\bar{X}_j) \pm [1.96 \times \sqrt{\frac{s_1^2}{n_1}}]$. This was done to establish possible normative values for cVEMP interpretation.

A corresponding T-stat at the 95% CI was calculated $(t_{stat} = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$, where $\bar{X}_j$ the weighted sample is mean of parameter j and S_j is the standard deviation of parameter j) to determine statistically significant differences in the weighted means of response parameters when compared to each other. If the 95% CI $(CI_{95\%} = (\bar{X}_1 - \bar{X}_2) \pm [1.96 \times \sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}])$ calculated from the difference between two compared weighted means did not enclose the value '0' within the 95% CI range, it was regarded as statistically significant. This corresponds with a p-value of < 0.05. These calculations were done to determine significant effects of stimulus type (click compared to tone burst) on cVEMP response parameters.

Likewise, weighted means were calculated and used with a two-sample t-test to determine the effect of SCM muscle activation method on CV and TBV results. A loop-calculation was used to compare the weighted means of the four different SCM muscle activation methods for CVs and five SCM muscle activation methods for TBVs. For example, the loop-calculation for SCM muscle activation methods of CVs compared the weighted means of each response parameter in the following order: *STC with SEH; STC with SETC; STC with SPF; SHE with SETC; SHE with SPF, and SETC with SPF.*

The effects of different transducers on response parameters were also determined for CVs and TBVs. Calculated weighted means of cVEMP response parameters were determined for studies using supra-aural headphones and compared to studies using insert earphones. Lastly, the effect of method to control SCM muscle EMG level on cVEMP response parameters were determined with a loop-calculation as indicated above for SCM muscle activation method.

Results

Systematic review

Five hundred and thirty-seven reports were initially identified with the database search and the procedural outcomes are indicated in Table 1. It was attempted to retrieve full text for 374 reports, which included some studies without control groups, since abstracts do not always indicate whether control groups were included or not. The full text for two reports were still in press and eight could not be retrieved, even when attempted to source them on other databases. From the 364 full text reports, 75 reports were initially included in the analysis. These 75 reports were included based on the aim of the study to determine the effects of stimulus and recording parameters on normal responses, and hence only studies where control group data were indicated or where the study per se determined normative data were included. Also, to limit the amount of variables, only studies where air-conducted tone burst or click cVEMPs over the SCM muscle in human adults (age 18–60) were measured, were included. The resulting excluded studies are systematically indicated in Table 1. Of all the remaining reports using click stimuli, two reports used a stimulus duration other than 0.1 ms (0.5 ms and 125 μsec) and one did not indicate the stimulus duration. They were excluded. For the tone burst group, two reports used a stimulus frequency other than 500 Hz (750 and 1000 Hz) and one did not indicate the stimulus frequency. They were also excluded. A final three reports in the tone burst group did not indicate stimulus level and were excluded.

Sixty-six reports remained and were included to be used for the meta-analysis. Twenty-four reports used 0.1-ms click stimuli exclusively, 36 used 500-Hz tone burst stimuli exclusively, and six reports used both of these stimuli. Thus, 30 reports were included for CVs and 42 for TBVs.

The stimulus and recording parameters of included reports are indicated in Supplementary Digital Content Table 1 available online

Table 1. Systematic review procedures of inclusion and exclusion.

	Number of reports
Database search results (DBSR)	537
DBSR excluding non-English reports	450
DBSR excluding duplicates	444
DBSR excluding reviews, letters, notes, dissertations or conference papers	408
DBSR excluding reports irrelevant to the study field	374
DBSR excluiding articles in press	372
DBSR excluding reports where full text is unavailable	364
DBSR excluding studies with no control group or studies where no normative data were indicated	221
DBSR excluding reports where participants were cochlear implanted	220
DBSR excluding reports where participant age was not indicated	207
DBSR excluding reports where participant age > 60	175
DBSR excluding paediatric reports	143
DBSR excluding animal studies	132
DBSR excluding oVEMP reports	118
DBSR excluding bone conduction reports	106
DBSR excluding galvanic stimulation reports	102
DBSR excluding logon stimulus reports	101
DBSR excluding skull tap reports	97
DBSR excluding reports where musculature other than SCM muscle used	95
DBSR excluding reports where response parameters were not clearly indicated or inconsistent with current study	76
DBSR excluding reports with abnormal recording conditions	75
DBSR excluding TBV reports with a stimulus frequency other than 500 Hz or stimulus frequency was not indicated	72
DBSR excluding CV reports with a stimulus duration other than 0.1 ms or stimulus duration was not indicated	69
DBSR excluding reports where stimulus level was not indicated	66

at http://informahealthcare.com/doi/abs/10.3109/14992027.2014.971468. Most reports used 95 dB nHL as stimulus level (10 CV reports and 31 TBV reports) and a stimulus rate of 5 Hz (17 CV reports and 32 TBV reports). The duration for CVs was kept at a constant of 0.1 ms and most TBV reports used a rise/fall and plateau time of 1 and 2 ms respectively (25 reports). Regarding recording parameters, the *supine, elevate head (SEH)* position was used most prevalently for both CVs and TBVs (16 CV reports and 19 TBV reports). Most CV reports used headphones (23 reports) while most TBV reports used insert earphones (25 reports). Only three CV reports indicated the amplifier gain values (1000, 2000 and 2500 Hz), but TBV reports mostly amplified input 5000 times (6 reports). Although a wide variety of filter settings was reported on, 20–2000 Hz were used most for CVs (11 reports) and TBVs (16 reports). Most reports indicated that EMG was visually monitored during cVEMP recording (16 CV reports and 22 TBV reports). Most prevalent stimulus and recording parameters in the systematic review are summarized in Table 2.

Since the meta-analysis would be done on the response parameters (latency P1, latency N1, raw amplitude, corrected amplitude, asymmetry ratio and threshold), the means for these parameters obtained from the participants in each study were carefully recorded underneath each heading. Where response parameters were indicated for the left and right ears separately, the mean of the two together was calculated and used for analysis (see Supplementary Digital Content Table 2 available online at http://informahealthcare.com/doi/abs/10.3109/14992027.2014.971468).

Table 2. Suggested stimulus and recording parameters of 0.1-ms click and 500-Hz tone burst cVEMPs.

	0.1-ms click cVEMP	*500-Hz tone burst cVEMP*
Stimulus parameters		
Level	95 dB nHL	95 dB nHL
Rate	5 Hz	5 Hz
Duration	0.1 ms	1 ms rise and fall, 2 ms plateau
Recording parameters		
Device	Across different devices	Across different devices
Positioning	Across different positions (ensure adequate SCM muscle contraction)	Across different positions (ensure adequate SCM muscle contraction)
Electrode montage	Active electrode: Upper half and middle third of SCM; Reference: Lateral end of upper sternum; Ground: forehead	Active electrode: Upper half and middle third of SCM; Reference: Lateral end of upper sternum; Ground: forehead
Transducer	Insert earphone	Insert earphone
Amplifier gain	5000	5000
Filter settings	20–2000 Hz	20–2000 Hz
Time window	50–100 ms	50–100 ms
Number of sweeps	256	256
Visual monitoring	Recommended: minimum level of 40 μV	Recommended: minimum level of 40 μV

Meta-analysis

Table 3 summarizes the weighted means, SDs and 95% CIs for CVs and TBVs. Concerning the effect of stimulus type on cVEMP results, a significant difference was evident between all response parameters of CVs and TBVs.

Table 4 indicates the weighted means, SDs and 95% CIs for CVs and TBVs for different SCM muscle activation methods. For CVs, the SCM muscle activation method had a statistically significant effect on latency P1 and N1, raw amplitude, corrected amplitude, and asymmetry ratio. Only when comparing the *SEH* and *STC* methods, the *STC* and *SPF*, and lastly the *SEH* and *SPF* methods for latency N1 were no significant differences noted. However, since the weighted latency N1 means of these methods were significantly different from all the other methods, it should rather be noted in a holistic fashion, that SCM muscle activation method has a significant effect on cVEMP latency N1 values. No comparisons could be made regarding effect of SCM muscle activation method on CV threshold values, since only the *SEH* method indicated these values.

For TBVs, statistically significant differences in the weighted means of each response parameter of the various SCM muscle activation methods were evident. Overall, the P1 and N1 latencies of TBVs are distinctly larger than those of CVs.

Table 5 shows the effect of transducer type on response parameters for CVs and TBVs. For CVs, 23 studies made use of a supra-aural headphone and five studies made use of insert earphones. A statistically significant effect of transducer type was indicated for latency P1, latency N1, asymmetry ratio and threshold. No comparisons could be made for raw amplitude, since only reports using a headphone indicated raw amplitude values. Corrected amplitude values were not indicated in any of the reports selected for determining the effect of transducer type.

A total of 13 studies in the TBV group used supra-aural headphones and 23 used insert earphones. One study did not indicate which transducer was used. Transducer type had a statistically significant effect on latency P1, latency N1, corrected amplitude, and asymmetry ratio. Only reports using insert earphones indicated threshold values, and could not be compared to reports using a headphone as transducer. It is worth noting that the latency values for TBVs are once again larger in comparison with those of CVs.

Table 3. Meta-analysis of weighted means between response parameters of 0.1-ms click and 500-Hz tone burst cVEMPs.

	Number of studies	*n*	*Weighted mean (SD)*	*95% CI*
Latency P1 (ms)				
0.1-ms click	26	660	12.19 (0.19)*	12.18–12.21
500-Hz tone burst	37	744	14.44 (0.20)*	14.42–14.45
Latency N1 (ms)				
0.1-ms click	26	660	19.90 (0.28)*	19.88–19.93
500-Hz tone burst	37	744	22.89 (0.39)*	22.86–22.92
Raw amplitude (μV)				
0.1-ms click	15	443	92.94 (11.18)*	91.90–94.00
500-Hz-tone burst	22	511	122.16 (13.82)*	120.97–123.36
Corrected amplitude				
0.1-ms click	2	24	2.61 (0.26)*	2.51–2.72
500-Hz tone burst	10	140	1.77 (0.10)*	1.75–1.78
Asymmetry ratio (%)				
0.1- ms click	10	258	14.06 (1.23)*	13.91–14.21
500-Hz tone burst	11	231	9.89 (1.27)*	9.73–10.05
Threshold (dB nHL)				
0.1-ms click	4	83	89.27 (0.88)*	89.08–89.46
500-Hz tone burst	8	228	81.02 (2.03)*	80.76–81.29

*$p < 0.05$. n = total number of participants in the indicated number of included studies. Participant age = 18–60 years. Asymmetry ratio = 100 × $(A_L - A_S)/(A_L + A_S)$, where A_L equals the larger P1-N1 amplitude and A_S equals the smaller P1-N1 amplitude.

Table 6 indicates the effect of method to control SCM muscle EMG level on cVEMP response parameters. For CVs, these methods included reports that indicated only rectifying cVEMP responses, only visually monitoring EMG level, and visually monitoring and rectifying cVEMP responses. Statistically significant differences can be seen for latency P1, latency N1, and asymmetry ratio. Only studies using the visual monitoring method indicated raw amplitude values, and no statistical inferences could be drawn. Likewise only studies using rectification alone indicated corrected amplitude values and only studies using the visual and rectifying methods indicated threshold values. No comparisons could be made for them.

The TBV group in Table 6 indicates that method to control SCM muscle EMG level has a significant effect on all cVEMP response parameters.

Discussion

A systematic review and meta-analysis was performed to determine the effect of stimulus type, SCM muscle activation method, transducer type, and method to control SCM muscle EMG level on cVEMP response parameters for participants between the ages of 18 and 60 years. The systematic review revealed most prevalent trends in stimulus and recording parameters which are suggested for clinical use. Relatively large sample sizes are included as a pooling result of the meta-analysis and normative values for cVEMP interpretation are suggested.

Most prevalent stimulus and recording parameters in the systematic review are summarized in Table 2 which correlates well with optimal parameters suggested by previous research: The stimulus level used most frequently in the systematic review was 95 dB nHL, which correlates well with 95–100 dB nHL and 90–95 dB nHL suggested for CVs and TBVs respectively by Akin and Murnane (2008). The indicated stimulus rate of 5 Hz for both CVs and TBVs was also suggested by Wu and Morufushi (1999) to be optimal. As suggested by Welgampola and Colebatch (2005), a 0.1-ms click seems to be used most which is reflected in the systematic review where only three reports out of the initial 24 CV reports indicated a different click duration. The previously suggested stimulus duration for TBVs is a 1-ms rise interval with a 2-ms plateau, while others prefer a two cycle rise and fall with no plateau (Zhou & Clarke Cox, 2004; Young, 2006; Wuyts et al, 2007; Welgampola & Colebatch, 2005). Cheng and Morufushi (2001a, 2001b) conducted studies specifically to determine optimal rise, fall, and plateau times and concluded that 1-ms rise and fall times combined with 2-ms plateau time would elicit the best possible 500-Hz VEMP responses. It is clear from Table 2 that this is preferred by most clinicians and is recommended for clinical use. Onset phase or polarity was not reported on regularly in the systematic review and only 21 of the 66 reports indicated using rarefaction.

The popular montage where electrodes are placed over the upper third or half of the SCM muscle (active) with the reference electrode over the lateral end of the upper sternum (Zhou & Clarke Cox, 2004; Cheng & Morufushi, 2001a, 2001b; Welgampola & Colebatch, 2001a) is confirmed in the meta-analysis. Although slightly diverse descriptions were given, most of them corresponded with the above-mentioned montage reported in literature.

Table 4. Meta-analysis of 0.1-ms click and 500-Hz tone burst cVEMP response parameters for different SCM muscle activation methods.

	0.1-ms click					*500-Hz tone burst*			
	Number of studies	*n*	*Weighted mean (SD)*	*95% CI*		*Number of studies*	*n*	*Weighted mean (SD)*	*95% CI*
Latency P1 (ms)					Latency P1 (ms)				
STC	5	213	13.06 (0.09)*	13.04–13.07	STC	11	331	14.63 (0.16)*	14.61–14.65
SEH′	15	341	11.75 (0.20)*	11.73–11.77	SEH′	19	296	14.05 (0.22)*	14.03–14.08
SETC	3	39	12.27 (0.12)*	12.24–12.31	SETC	3	41	14.18 (0.10)*	14.15–14.21
SPF	2	49	11.82 (0.10)*	11.79–11.85	SPF	2	31	15.24 (0.27)*	15.15–15.34
					SRH	1	20	15.1*	–
Latency N1 (ms)					Latency N1 (ms)				
STC	5	213	19.86 (0.19)*	19.84–19.89	STC	11	331	23.45 (0.40)*	23.41–23.49
SEH′	15	341	19.85 (0.35)*	19.81–19.89	SEH′	19	296	22.27 (0.37)*	22.23–22.31
SETC	3	39	20.43 (0.13)*	20.39–20.47	SETC	3	41	21.83 (0.35)*	21.72–21.94
SPF	2	49	19.91 (0.14)*	19.87–19.95	SPF	2	31	23.81 (0.54)*	23.62–24.00
					SRH	1	20	24.2*	–
Raw amplitude (μV)					Raw amplitude (μV)				
STC	3	166	36.01 (7.64)*	34.85–37.18	STC	7	195	130.82 (5.92)*	129.99–131.65
SEH′	11	259	112.70 (11.96)*	111.20–114.10	SEH′	7	134	137.94 (22.30)*	134.16–141.71
SETC	0	–	–	–	SETC	3	53	156.80 (13.11)*	153.72–160.33
SPF	0	–	–	–	SPF	1	20	70.58*	–
					SRH	2	40	123.6 (1.95)*	123.00–124.20
Corrected amplitude					Corrected amplitude				
STC	1	12	3.5*	–	STC	4	78	1.65 (0.05)*	1.64–1.66
SEH′	1	12	1.72*	–	SEH′	5	51	2.00 (0.13)*	1.97–2.04
SETC	0	–	–	–	SETC	0	–	–	–
SPF	0	–	–	–	SPF	1	11	1.5*	–
					SRH	0	–	–	–
Asymmetry ratio (%)					Asymmetry ratio (%)				
STC	3	138	10.80 (0.93)*	10.64–10.95	STC	4	173	4.96 (0.86)*	4.82–5.10
SEH′	3	74	20.19 (1.72)*	19.79–20.58	SEH′	5	68	16.78 (1.86)*	16.34–17.22
SETC	3	28	14.34 (0.46)*	14.16–14.51	SETC	2	30	17.75 (1.03)*	17.38–18.12
SPF	0	–		–	SPF	0	–	–	–
					SRH	0	–	–	–
Threshold (dB nHL)					Threshold (dB nHL)				
STC	0	–	–	–	STC	4	143	4.96 (0.86)*	4.82–5.10
SEH′	1	11	96	–	SEH′	0	–	–	–
SETC	0	–	–	–	SETC	1	20	104.35*	–
SPF	0	–	–	–	SPF	0	–	–	–
					SRH	0	–	–	–

*$p < 0.05$. n = total number of participants in the indicated number of included studies. Participant age = 18–60 years. Asymmetry ratio = 100 x $(A_L - A_S)/(A_L + A_S)$, where A_L equals the larger P1-N1 amplitude and A_S equals the smaller P1-N1. STC = Seated, turn head contralaterally. SEH = Supine, head elevated. SETC = Supine, elevate and rotate head contralaterally. SPF = Seated, push head forward. SRH = Supine, elevate and rotate head contralaterally.

A 50-ms time window was used by most CV reports in the systematic review (see Table 2). Eight TBV reports used a 60-ms time window and another nine used 100 ms. Since the entire SCM myogenic potential lasts about 40 ms and pre-stimulus recording time is necessary for determining estimated EMG level, a 50- to 100-ms time window is recommended (Zapala, 2007). The number of sweeps is generally between 64 and 256 and not more than 500 for each run or waveform (Zhou & Clarke Cox, 2004; Welgampola & Colebatch, 2005). This corresponded well with systematic review results where the maximum number of indicated sweeps was 512 for CVs and 256 for TBVs.

Artefact rejection is turned off, since muscle responses are considered artefacts when a signal average for neurogenic activity (commonly used in the clinic for cVEMPs) is used (Zapala, 2007). Filter settings are usually between 10 and 2000 Hz, since the dominant energy of EMG signals is between 40 and 150 Hz and amplifier gain is typically set at 5000 times (Zapala, 2007; Welgampola & Colebatch, 2005). Table 2 indicates that the majority of reports for both CVs and TBVs indicated using a 20–2000 Hz filter and amplifier gain of 5000 times.

The possible effect of stimulus type on response parameters has been a great point of interest in the study. Cheng et al (2003) reported that CVs revealed shorter latencies when compared to TBVs. Basta et al (2005) confirmed large differences between CV and TBV latencies and Wu et al (2007) substantiated these findings. Results of the meta-analysis (see Table 3) confirm the shorter latency for CVs in comparison to TBVs and also indicate that stimulus type had a significant effect on all response parameters. Tone burst duration

Table 5. Meta-analysis of 0.1-ms click and 500-Hz tone burst cVEMP response parameters for different transducers.

	0.1–ms click					*500–Hz tone burst*			
	Number of studies	*n*	*Weighted mean (SD)*	*95% CI*		*Number of studies*	*n*	*Weighted mean (SD)*	*95% CI*
Latency P1 (ms)					Latency P1 (ms)				
Headphone	19	521	12.25 (0.13)*	12.24–12.26	Headphone	14	189	13.95 (0.25)*	13.91–13.98
Insert earphone	5	120	11.63 (0.14)*	11.60–11.66	Insert earphone	23	555	14.61 (0.18)*	14.59–14.62
Latency N1 (ms)					Latency N1 (ms)				
Headphone	19	521	19.67 (0.20)*	19.65–19.68	Headphone	14	189	22.41 (0.54)*	22.34–22.49
Insert earphone	5	120	20.77 (0.46)*	20.69–20.85	Insert earphone	23	555	23.06 (0.32)*	23.03–23.08
Raw amplitude (μV)					Raw amplitude (μV)				
Headphone	12	388	94.47 (10.08)	93.47–95.47	Headphone	4	86	122.10 (11.34)	119.7–124.5
Insert earphone	0	–	–	–	Insert earphone	17	405	121.70 (14.65)	120.30–123.10
Corrected amplitude					Corrected amplitude				
Headphone	0	–	–	–	Headphone	7	84	1.58 (0.05)*	1.57–1.59
Insert earphone	0	–	–	–	Insert earphone	3	56	2.05 (0.09)*	2.03–2.08
Asymmetry ratio (%)					Asymmetry ratio (%)				
Headphone	8	224	12.38 (0.68)*	12.30–12.47	Headphone	3	29	14.45 (0.46)*	14.28–14.62
Insert earphone	2	60	25.12 (1.65)*	24.56–25.67	Insert earphone	8	212	9.26 (1.27)*	9.09–9.43
Threshold (dB nHL)					Threshold (dB nHL)				
Headphone	2	23	95.06 (0.27)*	94.95–95.17	Headphone	0	–	–	–
Insert earphone	2	60	51.00 (6.63)*	49.32–52.68	Insert earphone	8	228	81.02 (2.03)	80.76–81.29

*$p < 0.05$. n = total number of participants in the indicated number of included studies. Participant age = 18–60 years. Asymmetry ratio = $100(A_L - A_S)/(A_L + A_S)$, where A_L equals the larger P1-N1 amplitude and A_S the smaller P1-N1 amplitude.

(rise and fall time and plateau) alter latencies recorded, where an increase in duration leads to prolonged latencies (Cheng & Murofushi, 2001a, 2001b). Seeing that CV duration in the systematic review and meta-analysis was 0.1 ms and TBV duration much longer (most of the studies used a rise/fall time of 1 ms and a plateau of 2 ms), the overall increase in TBV latency is understood in terms of stimulus duration and confirms findings of previous reports.

Already in 1999 and 2001, Welgampola and Colebatch (2001a) and Murofushi et al (1999) illustrated that 500-Hz tone bursts evoke the largest VEMP amplitudes. These authors recommended the use of short tone bursts, since a large inter-laboratory variability concerning click-evoked cVEMP latency and amplitude was evident. Most recently, Viciana and Lopez-Escamez (2012) indicated that 500-Hz short tone bursts elicited consistently larger amplitudes. The meta-analysis in the current study concurred with these findings, where CVs had a weighted mean of 92.94 μV (11.18) and TBVs a larger weighted mean of 122.16 μV (13.82). A linear relationship between stimulus duration and cVEMP amplitude is confirmed by the meta-analysis, since the TBVs have a longer stimulus duration than CVs and TBV weighted amplitude means were larger than CV weighted amplitude means.

Most reports used visual EMG and/or μV level monitoring (see Supplementary Digital Content Table 1 available online at http://informahealthcare.com/doi/abs/10.3109/14992027.2014.971468). All reports applying monitoring used levels of more than 40 μV. Rosengren et al (2010) prescribe EMG levels of at least 40 μV and up to 150–200 μV. A minimum level of 40 μV for EMG monitoring is recommended in Table 2. Since a significant effect of method to control SCM muscle EMG level is noted on all response parameters in Table 6, care should be taken to perform one method only in the clinic. Also, since the reports in the systematic review and meta-analysis mostly represent the visual monitoring method, the suggested norms in Table 3 should be considered when performing this method to control SCM muscle EMG level (versus rectifying or the feedback method).

The meta-analysis indicated that the type of stimulus has a significant effect on AR. This is contrary to a study conducted by Bush et al (2010). Table 3 suggests upper limits of normality for CVs to be 14.21%, and 10.05% for TBVs (upper limit of normality = upper value of 95% CI, as determined statistically and not by simply adding two SDs). This is much less than the usual 30%–40% which is commonly used in clinical settings.

CV thresholds have been found to be within 75–85 dB nHL (Colebatch et al, 1994). Similarly, Welgampola and Colebatch (2001b) found a threshold range of 75–100 dB nHL (mean 89.6 ± 6.9) in a group with subjects ranging from 25 to 85 in age. The current meta-analysis suggested weighted threshold means of 89.27 dB nHL (SD 0.88) with a range of 89.08–89.46 to be accepted as normal for CVs (95% CI in Table 3).

For TBVs, the frequency tuning effect of the saccule leads to the lowest thresholds obtained in response to 500-Hz stimuli (Park et al, 2010; Tourtillott et al, 2010). This is also the stimulus frequency used in the meta-analysis and a weighted mean of 81.02 dB nHL (SD 2.03) with a range of 80.76–81.29 is suggested as normal. Zapala (2007) notes that thresholds obtained from left and right ears should be within 10 dB from each other to indicate normal results.

The number of reports for each method of SCM muscle activation method that was used for CVs and TBVs are indicated in Table 4. From the meta-analysis, it can be seen that the SCM muscle activation method had a significant effect on VEMP response parameters. Adequate SCM muscle contraction with similar EMG levels for both sides seems to be the most important outcome regarding positioning.

Not much is indicated in the literature regarding the effect of type of transducer used on cVEMP response parameters. The systematic review included reports where either a headphone or insert earphones were used. As can be seen from Table 5, a significant effect of

Table 6. Meta-analysis of 0.1-ms click and 500-Hz tone burst cVEMP response parameters for different methods to control SCM muscle EMG level.

	0.1-ms click					*500-Hz tone burst*			
	Number of studies	*n*	*Weighted mean (SD)*	*95% CI*		*Number of studies*	*n*	*Weighted mean (SD)*	*95% CI*
Latency P1 (ms)					Latency P1 (ms)				
Rectified	1	12	10.92 (0.00)*	–	Rectified	6	67	13.65 (0.08)*	13.63–13.66
Monitored	15	422	12.00 (0.12)*	11.99–12.01	Monitored	20	458	14.37 (0.04)*	14.36–14.37
Rectified and monitored	2	21	12.84 (0.08)*	12.87 – 12.80	Rectified and monitored	6	91	14.82 (0.10)*	14.80–14.83
					Feedback method	4	112	14.60 (0.05)*	14.59–14.61
Latency N1 (ms)					Latency N1 (ms)				
Rectified	1	12	19.55 (0.00)*	–	Rectified	6	67	21.27 (0.22)*	21.22–21.32
Monitored	15	422	19.78 (0.30)*	19.76–19.81	Monitored	20	458	22.91 (0.07)*	22.90–22.92
Rectified and monitored	2	21	21.02 (0.22)*	20.93–21.12	Rectified and monitored	6	91	23.04 (0.22)*	23.00–23.09
					Feedback method	4	112	23.34 (0.08)*	23.33–23.36
Raw amplitude (μV)					Raw amplitude (μV)				
Rectified	0	–	–	–	Rectified	1	18	90.70 (0.00)*	–
Monitored	9	268	92.17 (3.36)	91.77–92.57	Monitored	15	345	123.90 (3.81)*	123.50–124.30
Rectified and monitored	0	–	–	–	Rectified and monitored	0	–	–	–
					Feedback method	4	112	129.73 (2.45)*	129.28–130.18
Corrected amplitude					Corrected amplitude				
Rectified	1	12	1.72 (0.00)	–	Rectified	6	80	1.77 (0.05)*	1.76–1.78
Monitored	0	–	–	–	Monitored	0	–	–	–
Rectified and monitored	0	–	–	–	Rectified and monitored	4	60	3.28 (0.78)*	3.08–3.47
					Feedback method	0	–	–	–
Asymmetry ratio (%)					Asymmetry ratio (%)				
Rectified	1	12	34.5 (0.00)*	–	Rectified	3	31	21.59 (1.46)*	21.07–22.10
Monitored	5	115	16.34 (0.16)*	16.31–16.37	Monitored	5	128	7.91 (0.69)*	7.79–8.03
Rectified and monitored	0	–	–	–	Rectified and monitored	0	–	–	–
					Feedback method	3	61	10.76 (1.25)*	10.44–11.07
Threshold (dB nHL)					Threshold (dB nHL)				
Rectified	0	–	–	–	Rectified	0	–	–	–
Monitored	2	60	87.05 (0.01)	87.04 – 87.04	Monitored	5	146	85.50 (0.89)*	85.35–85.64
Rectified and monitored	0	–	–	–	Rectified and monitored	0	–	–	–
					Feedback method	3	61	73.46 (0.24)*	73.40–73.52

*$p < 0.05$. n = total number of participants in the indicated number of included studies. Participant age = 18–60 years. Asymmetry ratio = $100(A_L - A_S)/(A_L + A_S)$, where A_L equals the larger P1-N1 amplitude and A_S the smaller P1-N1 amplitude.

transducer type on cVEMP response parameters was found. Since the goal of cVEMP testing includes delivering high intensity sounds, insert earphones may prove to be a better option in order to prevent unwanted stimulus attenuation due to headphone displacement during testing.

Although latency does not clinically act as a function of stimulus level or tonic EMG obtained, which is probably due to the reflexive nature of the response (Colebatch et al, 1994), a statistically significant difference was noted for all response parameters with different methods to control SCM muscle EMG level. Thus, a standard method to control SCM muscle EMG level in the clinic is suggested.

Conclusion

Optimal stimulus and recording parameters have been suggested by previous research. The current systematic review and meta-analysis confirmed most of these findings by pooling results from a number of studies. Table 2 summarizes these parameters and they are suggested for clinical use as evidence-based practice. Response parameter values obtained from the meta-analysis covered a larger sample size than performed in any single study with weighted means and weighted standard deviations. Therefore, although not all stimulus and recording parameters were kept at a constant, the normative response values indicated in Table 3 are suggested as a guideline for cVEMP interpretation when using stimulus and recording parameters similar to those indicated in Table 2. Since stimulus type had a significant effect on latency values, CV and TBV are to be interpreted with their own set of suggested norms.

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Supplementary material

Supplementary Digital Content Tables 1 and II.