Cervical Vestibular-Evoked Myogenic Potentials in Sedated Toddlers

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Abstract

Introduction Cervical vestibular-evoked myogenic potentials (cVEMPs) are difficult to test in toddlers who cannot follow instructions or stay calm.

Objective Due to the growing need for vestibular testing in very young children as a part of a delayed walking assessment battery, this study aimed to provide a solution to this problem by recording the cVEMPs in toddlers during sedation.

Method The cVEMPs measures were assessed in 30 toddlers aged 12 to 36 months with normal motor milestones. They were sedated with chloral hydrate. Then, the head was retracted $\sim 30^{\circ}$ backward with a pillow under the shoulders, and turned 45° contralateral to the side of stimulation to put the sternocleidomastoid (SCM) muscle in a state of tension.

Results The P13 and N23 waves of the cVEMPs were recordable in all sedated toddlers. The cVEMPs measures resulted in the following: P13 latency of 17.5 ± 1.41 milliseconds, N23 latency of 25.58 ± 2.02 milliseconds, and peak-to-peak amplitude of 15.39 ± 3.45 μV. One-sample *t*-test revealed statistically significant longer latencies and smaller amplitude of the toddlers' cVEMPs relative to the normative data for adults.

Conclusions The difficulty of cVEMPs testing in toddlers can be overcome by sedating them and attaining a position that contracts the SCM muscle. However, the toddlers' recordings revealed delayed latencies and smaller amplitudes than those of adults.

Keywords

- cervical vestibular-evoked myogenic potentials
- chloral hydrate
- saccule

Introduction

Most vestibular disorders in infants and young children manifest not as vertigo or dizziness, but as balance problems and/or developmental delay of motor milestones. Early identification of such disorders is necessary for early intervention.[1] It is important to consider a time-efficient, non-invasive, accurate, and comfortable test battery for vestibular assessment that is appropriate for children of all ages. However, selecting tests that are appropriate for use with the pediatric population is a great challenge. Many studies have focused mainly on the application and adaptation of adult tests such as video-nystagmography, computerized dynamic posturography, rotary chair, and cervical vestibular-evoked myogenic potentials (cVEMPs).[2–4] Typically, children in these studies were aged 5 years or older, with the exception of the new normative cVEMPs data, wich covers age ranges from a few days through the teen years.[3,5–11]

Cervical vestibular-evoked myogenic potentials testing is applicable to all subjects, and is gradually becoming a part of the standard vestibular assessment in many clinics. It is a short-latency electromyographic (EMG) response evoked mainly by loud acoustic stimuli. Sound-induced vibrations of the perilymph within the saccule are thought to give rise to the cVEMPs. The saccular afferent conduction passes through the inferior vestibular nerve to the medial vestibular nucleus.

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The vestibulo-collic tract then carries an inhibitory response via the motor neurons of the 11th cranial nerve to the cervical flexor motor neurons. The cVEMPs are measured from the ipsilateral sternocleidomastoid (SCM) muscle while the muscle is activated.[12–14]

Adaptations of adult cVEMPs have been previously described for use with children.[1,3,15–17] However, these have not been widely used on either a research or clinical basis. One procedure is to standardize the level of SCM muscle contraction by target monitoring of EMG activity using an extra neck electrode. Applying this electrode to children is not feasible because of their small necks, but it is possible to calculate the asymmetry ratios or the normalized amplitude from raw amplitude measures. Other cVEMPs adaptations include placing the child on a parent's lap, having the child focus on a cartoon film to maintain head turn for muscle contraction, positioning the child for simultaneous bilateral recording, using 500 Hz stimuli to obtain a more robust waveform, and continuous positive reinforcement.

However, the following are intrinsic problems involved when taking cVEMPs measures in very young children who cannot cooperate: 1) young children have poor muscle tone compared with grown children and adults; 2) maintaining neck muscle contraction is difficult and often requires several interruptions of the recording session; 3) the time required to educate parents on their need to help during the test, combined with the previously mentioned difficulties, leads to longer recording sessions; and 4) a technician is needed to position the subjects and control the muscle contraction level.[5,18]

Furthermore, restlessness and crying are common situations encountered when dealing with infants and young children. These children cannot be effectively tested unless sedated. Chloral hydrate is the most frequently used sedative in pediatric patients, with successful sedation in 85–98% of children. Despite the availability of newer agents, chloral hydrate remains a common choice.[19,20] Chloral hydrate induces sleep at minimal doses. Patients under its influence maintain normal reflexes, and sleep can be interrupted by pain or lesser disturbances.[19] At therapeutic doses, it produces sedation without significant adverse effects on the cardiovascular or respiratory functions.[20] Chloral hydrate is regarded as a relatively poor muscle relaxant. Muscle flaccidity appears only with chloral hydrate overdose. Other overdose symptoms include hypothermia, cardiac arrhythmias, and respiratory depression.[19] The goal of our study was to test the producibility of cVEMPs under chloral hydrate sedation in normal toddlers while assuming a position that keeps the SCM muscle contracted. The aim was to standardize cVEMPs parameters in sedated normal toddlers to make testing available for those with delayed motor milestones or suspected vestibular impairment.

Method

Subjects

This study included 30 toddlers, 18 females (60%) and 12 males (40%), aged from 12 to 36 months (mean age ± standard deviation [SD]: 21.27 ± 8.48 months). All toddlers studied had delayed language development and/or risk of hearing loss (due to family history or pre, peri or postnatal insults). They were referred to the audiology unit at the Faculty of Medicine, Zagazig University for an audiological evaluation and follow-up. The cVEMPs were recorded while the children were under chloral hydrate sedation during an auditory brainstem response (ABR) assessment for threshold detection. Those with an abnormal ABR threshold were excluded to avoid the possibility of associated congenital vestibular disorder. The parents of all children provided written consent to perform the cVEMPs recording. The work period spanned from January 2015 to January 2016. The Institutional Review Board renewed its approval in January 2016.

Procedure

All children were subjected to a full history taking, which included gestational age at birth, birth weight, pre, peri or postnatal insults, motor milestones and family history. Children with a history of respiratory distress syndrome, low birth weight, delayed motor milestones, or cerebral palsy were excluded from the study. This was followed by an otoscopic examination to ensure normal appearance and mobility of the tympanic membrane. Normal middle ear functions were assessed using middle ear analyzer Madsen (model Zodiak 902, USA). Hearing in all subjects was normal in the 2–4 kHz frequency range (right ears: 23.57 ± 8.42 dBnHL; left ears: 23.33 ± 8.16 dBnHL), as measured with ABR via an auditory evoked potential system model Smart EP, version 2.39 (Intelligent Hearing Systems, Miami, Florida, USA). To study the effect of maturation on cVEMPs measures, the research group was divided into two age subgroups: subgroup I (ages 12 to 24 months) and subgroup II (ages 24 to 36 months).

Cervical Vestibular-Evoked Myogenic Potential Recording

Cervical vestibular-evoked myogenic potentials were recorded from both the right and left sides using cup-shaped scalp electrodes. The electrode sites were cleaned with alcohol and scrubbed with an abrasive gel to keep the electrode impedance below 3 kΩ. The cleaning was done prior to the administration of the sedative to avoid the interruption of sleep after sedation. An active electrode was placed at the junction between the middle and the upper thirds of the ipsilateral SCM muscle. The reference electrode was attached on the upper sternum. The ground electrode was placed on the forehead, the same location as the ABR threshold detection montage. All children were sedated with chloral hydrate at a dose of 25 mg/kg, and, if necessary, a second dose of 25 mg/kg was administered after 30 minutes. The maximum total dosage was 50 mg/kg.[21] The children slept in the supine position on a testing table. The child's head was kept retracted 30° backward and turned 45° to the opposite side of stimulation using a special pillow below the shoulders to put the muscle in a state of tension.

Air-conducted 500 Hz tone bursts consisting of 1 millisecond raise/fall time and 2 milliseconds plateau time were delivered monaurally to both ears through TDH-39

headphones at an intensity of 100 dBnHL and a rate of 5/s. At least two trials of 100 sweeps were averaged to check test wave repeatability. The amplifier gain was set to 5K. A 10 Hz to 3,000 Hz band-pass filter was used. The analysis time was 56 milliseconds. Cervical vestibular-evoked myogenic potentials recordings were identified visually as biphasic EMG potentials with an initial positive deflection wave (P13) followed by a negative deflection wave (N23).[22] The peak latencies of waves P13 and N23, the peak-to-peak amplitude and the interaural amplitude difference (IAD) ratio were measured. The ratio was calculated as follows:

$$(A\,R - A\,L)/(A\,R + A\,L),$$

where AR and AL are the peak-to-peak amplitude (p13 to n23) on the right and left sides respectively.[23]

Statistical Analysis

Data obtained from this study were analyzed using the SPSS software statistical computer package, version 21. The assumption of normality was checked using Shapiro-Wilk's test for normality, which revealed a normal distribution for latency, amplitude, and IAD parameters ($p > 0.05$).[24,25] After a normality confirmation, the parametric statistics were applied. Simple descriptive analysis was performed to calculate the mean (X) and standard deviations ($\pm$SD) of the test variables. A comparison of test variables in different categories and subgroups was performed using paired-sample, independent-sample, and one-sample *t* tests.

Results

Biphasic cVEMPs responses (P13 and N23 waves) were detectable and replicable across all subjects involved in this study. As shown in ►**Table 1**, paired samples *t* test revealed no significant differences between the cVEMPs responses from the right and left sides ($p > 0.05$). Therefore, the results of the right and left ears were combined into one group. In ►**Table 2**, the results of the independent-sample *t* test showed no significant differences in the cVEMPs measures between males and females and between the two age subgroups ($p > 0.05$). The recorded cVEMPs responses of two subjects, one 16-month-old boy (age subgroup I) and one 31-month-old girl (age subgroup II), are shown in ►**Fig. 1**.

Based on our evaluation of 30 toddlers under sedation with special head positioning, normative values (X $\pm$ SD) and 95% confidence intervals (95%CI) for the cVEMPs measures were established (►**Table 3**). In comparison to adult normative data, collected using the same equipment,[26] the one-sample *t*-test revealed statistically significant longer P13 and N23 latencies and statistically significant smaller peak-to-peak amplitude of the toddlers' cVEMPs ($p \leq 0.05$). Furthermore, the IAD did not differ significantly in our group in comparison to that of adults ($p > 0.05$) (►**Table 3**).

Discussion

The muscle tone of infants and young children is poor compared with that of grown children and adults. However, it is possible to record cVEMPs from the SCM during infancy and early childhood. There is ample literature addressing cVEMPs recording in children as young as 2–16 days during natural sleep,[7,9] 4 weeks,[10] 1–12 months,[5] and $\geq$ 3 years.[3,6,8,11] To our knowledge, no studies are concerned with cVEMPs recording during the age range of 1 to 3 years, the period in which walking difficulties appear in children. In a trial to overcome the difficulty in cVEMPs recording in very young children who cannot follow the instructions of the examiner, the current study was designed to test the producibility of cVEMPs under sedation, while assuming a head position that maintains the SCM contracted and to set the normative values of the latencies, the amplitude, and the amplitude ratio.

Because muscle tone and reflexes during the non-rapid eye movement sleep are slightly reduced or even similar to wakefulness,[27] cVEMPs could be recorded during sleep.[7,9] Moreover, as chloral hydrate is a relatively poor muscle relaxant with no diminution of normal reflexes when used in minimal doses,[19] we hypothesized that cVEMPs could be recorded in young children under sedation with minimum doses of chloral hydrate.

Identifiable and reproducible biphasic cVEMPs were recorded from the SCMs of all toddlers examined. The current results support and expand the previous findings that reproducible cVEMPs can be recorded in very young children.[3,5–11] All cVEMPs measures, in the present study, exhibited fairly normal distributions regarding side, age, and sex subgrouping.

In electrophysiologic tests, the symmetry of measures between both sides is of great value. Comparing the cVEMPs

Table 1 Mean, standard deviations, and paired-samples *t*-test results of right versus left cVEMPs measures

cVEMPs measures	Right ($n = 30$)		Left ($n = 30$)		*t* (*p*)
	X	$\pm$ SD	X	$\pm$ SD	
P13 latency (in ms)	17.66	1.22	17.34	1.61	0.860 (0.404)
N23 latency (in ms)	25.21	1.90	25.94	2.13	−1.025 (0.323)
Amplitude (in μV)	15.97	3.08	14.81	3.80	1.359 (0.197)

Abbreviations: cVEMPs, cervical vestibular-evoked myogenic potentials; n, number of ears; SD, standard deviation; *t* (*p*), t-value and its probability; X, mean values.

Table 2 Mean, standard deviations, and independent-sample *t* test results of males versus females and the two age subgroups' cVEMPs measures

cVEMPs measures	Gender			Age		
	Males ($n = 24$) X ± SD	Females ($n = 36$) X ± SD	*t* (*p*)	Age subgroup I ($n = 36$) X ± SD	Age subgroup II ($n = 24$) X ± SD	*t* (*p*)
P13 latency (in ms)	17.41 ± 0.88	17.56 ± 1.7	−0.292 (0.772)	17.42 ± 1.71	17.62 ± 0.82	−0.347 (0.711)
N23 latency (in ms)	25.92 ± 1.82	25.35 ± 2.16	0.743 (0.464)	25.46 ± 1.96	25.75 ± 2.18	−0.374 (0.711)
Amplitude (in μV)	16.87 ± 2.70	14.40 ± 3.6	2.025 (0.056)	14.67 ± 3.35	15.88 ± 3.53	−0.927 (0.362)
IAD	−0.007 ± 0.09	0.081 ± 0.13	−1.386 (0.189)	0.06 ± 0.13	0.03 ± 0.12	0.488 (0.634)

Abbreviations: cVEMPs, cervical vestibular-evoked myogenic potentials; IAD, interaural amplitude difference; n, number of ears; SD, standard deviation; *t* (*p*), t-value and its probability; X, mean values.

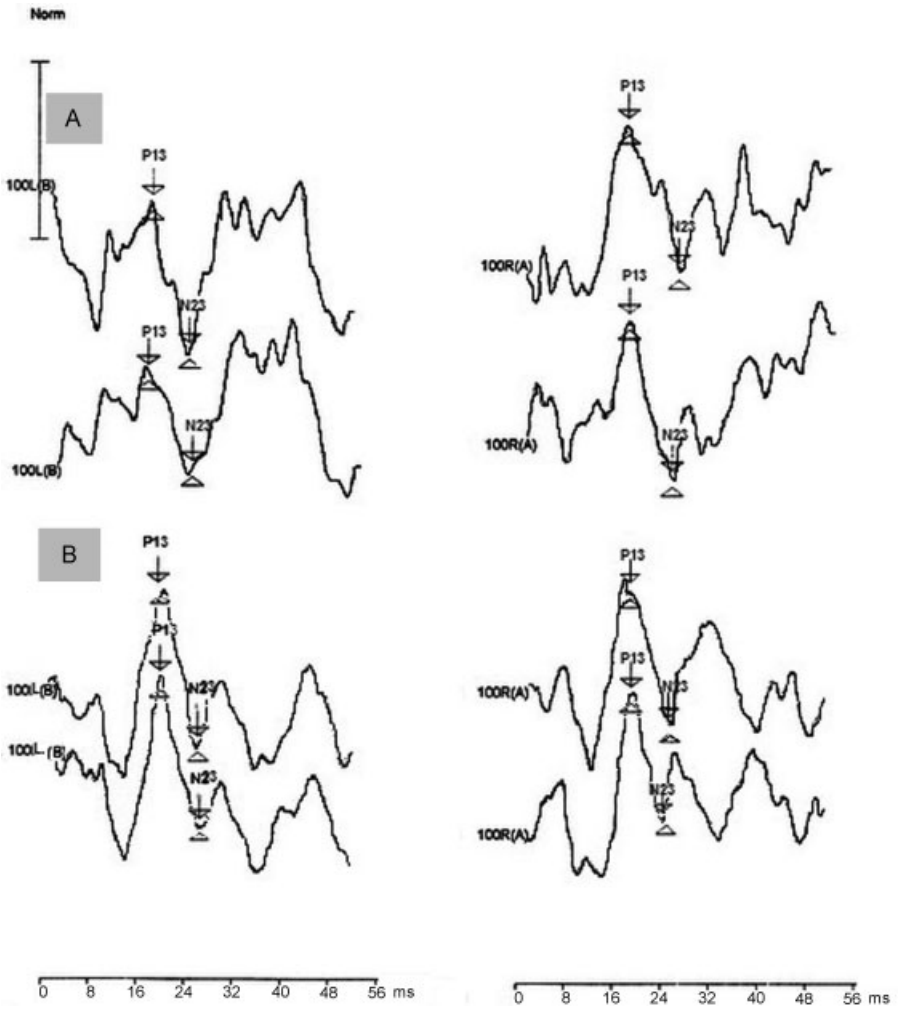

Fig. 1 Representative illustration of the biphasic cVEMPs waveforms (P13 and N23) recorded from two toddlers in response to 500 Hz tone bursts at an intensity of 100 dBnHL. (A) Bilateral responses obtained from a 16-month-old boy (age subgroup I). (B) Bilateral responses obtained from a 31-month-old girl (age subgroup II). No differences can be observed when comparing the right and left sides, the sex and the different age subgroups (I and II).

Table 3 Normative values (mean ± SD) and 95% confidence intervals for cVEMPs responses collected from sedated toddlers and compared with adult values using the one-sample *t*-test

cVEMPs measures	Toddlers ($n = 60$)	95% confidence intervals		Adults[26] ($n = 40$)	*t* (*p*)
	X ± SD	Lower	Upper	X ± SD	
P13 latency (in ms)	17.50 ± 1.41	16.98	18.03	13.17 ± 0.90	16.83 (0.000)
N23 latency (in ms)	25.58 ± 2.02	24.82	26.33	22.53 ± 1.15	8.271 (0.000)
Amplitude (in μV)	15.39 ± 3.45	14.10	16.68	69.03 ± 9.64	85.16 (0.000)
IAD	0.05 ± 0.13	−0.024	0.116	0.0077 ± 0.134	1.178 (0.630)

Abbreviations: cVEMPs, cervical vestibular-evoked myogenic potentials; IAD, interaural amplitude difference; n, number of ears; SD, standard deviations; *t* (*p*), t-value and its probability; X, mean values.

measures from right versus left sides reflects symmetry of saccular function. The lack of such symmetry could be an indication of unilateral vestibular deficit. Symmetrical P13 and N23 peak latencies and peak-to-peak amplitude were obtained in this study by comparing measures from the right and left sides. These findings are in agreement with the earlier cVEMPs research outcomes.[3,8,11] The vestibulo-collic reflex generating the cVEMPs response originates from the lower brainstem, which has a little laterality effect. Consequently, the symmetry of the data indicates the coordinated activity of the vestibular system on both sides.

Comparisons of cVEMPs measures for both male and female toddlers revealed no significant sex differences, a finding that is in agreement with those of other studies.[3,11] This could be related to a relatively similar neural length and conduction velocity during these earlier ages.

Another important finding is the comparable cVEMPs measures between the two age subgroups involved in this study. Our results are supported by other studies that investigated younger and older children. In a study involving the younger age group, Young et al reported a significant reduction of P13 latency from the 3rd to the 4th days after birth, which then became constant during the 5th through the 13th days.[9] Unlike P13 latency, N23 latency and peak-to-peak amplitude remained stable from the 3rd to 15th days. In addition, Valente and Picciotti et al reported this stability in the cVEMPs latency and amplitude measures in older children (> 3 years).[3,8] The conduction delay noted during the first few days of life could be due to hypo-myelination, which lowers the conduction velocity along the sacculo-collic reflex pathway. This is followed by the rapidly progressive myelination that characterizes functional systems, including the vestibular system.[28] The lack of a significant age effect in the current study reveals that the maturation of the sacculo-collic reflex pathway is growing very slowly during this period.

On the contrary, Kelsh et al reported a shorter N23 peak latency in the younger children subgroup (3–5 years) in comparison with the older children subgroup (> 5 years) (significant in the left side only) using click stimuli.[6] In addition, El-Danasoury et al detected significant P13 and N23 peak latencies prolongation and amplitude enhancement with the progress of age from 5 to 12 years using click stimuli.[11] They attributed this prolongation of latencies with age to the increase in the head and neck dimensions with age, whereas the amplitude increase was related to the greater tonic strength of the SCM as age increases.

When compared with adult norms, our toddler group's cVEMPs exhibited statistically significant longer peak latencies. This was controversial in comparison with other studies that reported shorter latencies in children as a result of the age effect.[3,6,11] We attribute this controversy to the use of chloral hydrate sedation in the children tested, and to the relatively different head position. Furthermore, we assume a stronger strengthening of the synapses involved in the reflex arc and proper wiring in adults. On the other hand, Picciotti et al found no significant difference in p13 or n23 latencies in children when compared with adults.[8] They suggested a complete development of the vestibular structures in 3 year-old children to address this outcome.

In agreement with El-Danasoury et al, we found in children a statistically significant smaller peak-to-peak amplitude than in adults.[11] This finding can be explained by the smaller muscle bulk of toddlers in comparison to adults, and the minimal muscle relaxation induced by sedation. However, Valente and Picciotti et al found no significant age effect on the amplitude.[3,8] Moreover, the IAD value revealed no age-related difference in this study, similar to that of Picciotti et al.[8] This relative value reduces the marked intersubject variability of the absolute amplitude measure. Because of this variability in findings in the literature, we encourage each center to develop its own age-related normative data.

Conclusion

The cVEMPs were recorded successfully in normal toddlers under chloral hydrate sedation, while assuming a position that keeps the SCM muscle contracted. In comparison to normative adult data, toddlers had delayed latencies and a smaller amplitude. There were no effects of age, sex, or side on the cVEMPs recordings of the tested group. Variable cVEMPs measures were found among different laboratories,

and that reveals the need for each laboratory to develop its own pediatric normative data.

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