REVIEW DERLEME

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Vestibular Evoked Myogenic Potentials with Compressed High-Intensity Radar Pulse Stimuli: A Literature Review

Sıkıştırılmış Yüksek Yoğunluklu Radar Titreşimi Uyaranıyla Vestibüler Uyarılmış Miyojenik Potansiyeller: Literatür Derlemesi

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ABSTRACT Vestibular evoked myogenic potentials (VEMPs) are commonly used noninvasive electrophysiological test methods in clinics. VEMPs are short-latency muscle reflex responses triggered by stimulation of peripheral otolith organs. The inhibitory myogenic response measured over the sternocleidomastoid muscle is cervical VEMP (cVEMP); the excitatory myogenic response measured over the extraocular muscles, the inferior oblique, is the ocular VEMP (oVEMP). cVEMP is characterized by a biphasic wave in the form of one positive peak (P1/P13) occurring at an average of 13th milliseconds and one negative peak (N1/N23) occurring at an average of 23rd milliseconds. oVEMP is characterized by a biphasic wave in the form of one negative peak (N1/N10) occurring at an average of 10th milliseconds and one positive peak (P1/P16) occurring at an average of 16th milliseconds. Stimulus type affects the VEMP findings. Click stimulus was first used in VEMP studies. The stimulus that effectively stimulates the otolith organs and generates the highest amplitude waves is being investigated. 500 Hertz (Hz) tone burst stimulus is more effective than click stimulus in VEMP tests and its clinical use has become widespread. Compressed high-intensity radar pulse (CHIRP) is an acoustic stimulus that is effective in auditory electrophysiology. VEMP in responses to CHIRP stimulus was reported in recent studies. In this review, the findings of studies examining VEMP responses triggered by CHIRP stimuli are integrated. The aim of this review is to evaluate whether the CHIRP stimulus is an effective stimulus in VEMP tests.

Keywords: Vestibular evoked myogenic potentials; cervical vestibular evoked myogenic potentials; ocular vestibular evoked myogenic potentials; compressed high-intensity radar pulse

ÖZET Vestibüler uyarılmış miyojenik potansiyeller [vestibular evoked myogenic potentials (VEMP)], ses, titreşim veya elektriksel stimülasyonla periferik otolit organların uyarılması sonucu tetiklenen kısa latanslı kas refleks cevaplarıdır. VEMP klinikte yaygın olarak kullanılan noninvaziv elektrofizyolojik test yöntemidir. Sternokleidomastoid kas üzerinden ölçülen inhibitör miyojenik yanıt servikal VEMP (sVEMP); inferior oblik üzerinden kaydedilen eksitatör miyojenik yanıt oküler VEMP (oVEMP) olarak adlandırılır. sVEMP 13. milisaniyede ortaya çıkan bir pozitif tepe (P13/ P1), ortalama 23. milisaniyede ortaya çıkan negatif tepe (N23/N1) şeklinde bifazik dalga formu ile karakterizedir. oVEMP, 10. milisaniyede ortaya çıkan negatif tepe (N10/N1) ile 16. milisaniyede ortaya çıkan pozitif tepe (P16/P1) şeklinde bifazik dalga formu ile karakterizedir. sVEMP bulgularında P1, N1 latansları, P1-N1 dalga amplitüdü değerlendirilir. oVEMP bulgularında N1, P1 latansları, N1-P1 dalga amplitüdü değerlendirilir. Kullanılan uyaranın türü VEMP bulgularını etkiler. İlk VEMP çalışmalarında klik uyaran kullanılmıştır. Otolit organları en etkili şekilde uyaran ve yüksek amplitüdlü dalgalar oluşturan uyaran araştırılmaktadır. VEMP testlerinde 500 Hertz (Hz) tone burst (TB) uyaranının klik uyarana göre daha etkili bir uyaran olduğu gösterilmiştir. 500 Hz TB uyaranının klinik kullanımı yaygınlaşmıştır. Sıkıştırılmış yüksek yoğunluklu radar titreşimi [compressed high-intensity radar pulse (CHIRP)], işitsel elektrofizyolojide etkili olduğu gösterilen akustik bir uyarandır. CHIRP uyaran, son yıllarda, VEMP testlerinde kullanılmaya başlanmıştır. Bu derlemede, CHIRP uyaranla tetiklenen VEMP yanıtlarını inceleyen çalışmaların bulguları entegre edilmiştir. Bu derlemenin amacı, CHIRP uyaranın VEMP testlerinde etkili bir uyaran olup olmadığını değerlendirmektir.

Anahtar Kelimeler: Vestibüler uyarılmış miyojenik potansiyeller; servikal vestibüler uyarılmış miyojenik potansiyeller; oküler vestibüler uyarılmış miyojenik potansiyeller; sıkıştırılmış yüksek yoğunluklu radar titreşimi

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Vestibular evoked myogenic potentials (VEMPs) are muscle reflex responses triggered by stimulation of the utricle [ocular VEMP (oVEMP)] and saccule [cervical VEMP (cVEMP)]. cVEMP was first described by Colebatch et al. in 1994.[1] cVEMP responses assessed vestibulocolic reflex arc, saccular function, and inferior vestibular nerve. The afferents of the vestibulocolic reflex arc extend from the saccule to Scarpa's ganglion, inferior vestibular nerve, and the medial and lateral vestibular nuclei. The efferents of the vestibulocolic reflex arc extend from the vestibular nuclei to medial and lateral vestibular nuclei and the accessory nerve. oVEMP was first described by Rosengren et al. in 2005.[2] oVEMP responses, assessed utricular function, superior vestibular nerve, and vestibulo-ocular reflex arc. The afferents of vestibulo-ocular reflex arc extend from the utricle to Scarpa's ganglion, superior vestibular nerve, and the vestibular nuclei. The efferents of vestibulo-ocular reflex arc extend from the vestibular nuclei to the motor neurons of the oculomotor and trochlear cranial nerves.[3]

The sensitivity of the vestibular organs to high-intensity acoustic stimuli has long been known. Tullio initiated research showing the sensitivity of the vestibular system to auditory stimuli in 1929. Tullio constitutes the fenestration of bony labyrinth in experimental animals. The motion of labyrinth fluids, and eye movements caused by the acoustic stimulus were observed.[4] Bekesy observed vestibular responses triggered by acoustic stimuli, independent of the cochlea.[5] Bickford et al. identified short-latency myogenic potentials recorded on the inion in response to a high-intensity click stimulus.[6] In a subsequent study, it has been shown that the peripheral source of the inion potential is the saccule.[7] In 1992, Colebatch and Halmagyi recorded short latency myogenic potentials in response to high-intensity click stimulus with an electrode placed on the contracted sternocleidomastoid muscle (SCM).[1,8] Air-conducted VEMP is initially triggered by click stimuli. Subsequently, tone bursts replaced click stimuli, and they have become commonly used stimuli. Tone bursts are frequency-specific tonal stimuli. Since the stimulation duration is longer, tone bursts transmit more energy to the inner ear. Higher response rates and higher amplitude values were obtained with a 500 Hertz (Hz) tone burst stimulus. 500 Hz tone burst stimulus has been frequently used in VEMP testing.[9] In the VEMP tests, the compressed high-intensity radar pulse (CHIRP) stimulus has been used in recent years. In this review, VEMP studies in which CHIRP stimuli are evaluated are inspected.

CHIRP STIMULI

Shore and Nuttal used tone burst stimuli with exponentially increasing frequency in 1985.[10] Expanding this concept, Dau et al. described the CHIRP stimulus in 2000.[11] Due to the temporal distribution of the frequencies, CHIRP stimuli provide simultaneous depolarization of the basilar membrane, the maximum firing of the nerve, and higher amplitude responses. The frequency of CHIRP stimuli changes over time. If it increases over time, it is called up-CHIRP; if it decreases over time, it is called down-CHIRP. Elberling et al. developed a Claus Elberling CHIRP (CE-CHIRP) stimulus with a click stimulus spectrum, the frequency of which varies from low to high.[12] Then, as an alternative to tone burst stimuli, frequency-specific narrowband CE-CHIRP stimulus was proposed at 500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz. In 2010, CE-CHIRP stimuli of different stimulus durations and different intensity levels were compared. It has been stated that short stimulus duration is appropriate for high-intensity stimuli and long stimulus duration is appropriate for low- and moderate-intensity stimuli. A level-specific (LS) CE-CHIRP stimulus has been developed, depending on the intensity level (designed differently for each 5 dB in the 0-100 dB range).[13,14] In addition, frequency-specific narrowband LS CE-CHIRP stimuli are available, 500 Hz, 1,000 Hz, 2,000 Hz, and 4,000 Hz.

CVEMPS RESULTS WITH CHIRP STIMULI IN HEALTHY INDIVIDUALS

There are ten cVEMP studies in which a CHIRP stimulus is evaluated in the literature (Table 1). The first study in which the CHIRP stimulus was evaluated in the cVEMP test was conducted by Wang et al. in 2014.[15] Different types of CHIRP stimuli have been used in the literature such as 500 Hz CHIRP, 500 Hz CE-CHIRP, 500-4,000 Hz CE-CHIRP, CW-

TABLE 1: Cervical vestibular evoked myogenic potentials studies in which CHIRP stimulus is evaluated.[21]

	Publication year	Number of healthy controls	Number of patienta	Mean age of participanta	CHIRP type	Compared stimulus	Stimulus intensity level (dB)	Response rate of CHIRP (%)	Response rate of compared stimulus (%)	CHIRP P1 latency (ms)	Compared stimulus P1 latency (ms)	CHIRP N1 latency (ms)	Compared stimulus N1 latency (ms)	CHIRP amplitude CH (μV)	Compared stimulus amplitude OS (μV)	CHIRP normalized amplitude (μV)	Compared stimulus normalized amplitude (μV)	CHIRP threshold CH (dB)	Compared stimulus threshold (dB)
Wang et al.[15]	2013	30	-	24	500 Hz CE-CHIRP	Tone pip	100	100	100	4.905	11.812	11.877	19.1	14.422	13.334	-	-	-	-
Özgür et al.[19]	2015	39	-	28	500-4,000 Hz CHIRP	500 Hz TB	100	89.7	93.5	9.9	15.8	-	-	33	93.5	-	-	-	-
Walther and Cebulla[22]	2016	10	-	37.5	CW-VEMP-CHIRP	500 Hz TB	100	90	90	-	-	-	-	233	183.2	-	-	-	-
Cebulla and-Walther[26]	2019	5	-	38.6	CW-VEMP-CHIRP	-	100	85	-	15.1	-	23.7	-	237	206	-	-	-	-
Moinudeen et al.[23]	2020	30	-	22	500 Hz CHIRP	500 Hz TB	100	-	-	12.61	16.4	18.71	22.36	70.15	68.45	-	-	-	-
Murofushi et al.[18]	2020	-	16	42.9	LS CE-CHIRP	TB	100	81.2	81.2	14.52	18.1	23.6	28.4	-	-	0.44	0.91	-	-
Ocal et al.[21]	2021	50	-	26.7	360-720 Hz CE-CHIRP	500 Hz TB	100	100	100	10.46	16.04	19.21	25	54.95	53.58	-	-	-	-
Mat et al.[16]	2021	31	-		500 Hz NB CE-CHIRP	500 Hz TB	95 dB nHL	-	-	**11.92***	**14.17***	**21.25***	**23.67***	-	-	**1.17***	**0.97***	-	-
Aydın et al.[16]	2022	56	-	34.6	250-10,900 Hz CHIRP	500 Hz TB	105	96.4	92.8	10.40	13.95	18.62	22.21	62.63	55.43	1.38	1.2	-	-
Aydın and Erbek.[18] Controls	2022	54		40.9	500 Hz LS CE-CHIRP	500 Hz TB	100	98	97	12.42	16.05	21.56	25.93	102.63	121.66	1.45	1.52	82.17	83.71
Aydın and Erbek.[18] Patients	2022		50	53.3	500 Hz LS CE-CHIRP	500 Hz TB	100	96	93.5	12.14	11.88	20.88	24.98	72.77	70.92	1.06	1.02	88.01	89.13

*Median values (not included in the averages); CHIRP: Claus Elberling Compressed high-intensity radar pulse; CE-CHIRP: Claus Elberling CHIRP; VEMP: Vestibular evoked myogenic potential; LS: Level-specific; TB: Tone burst.; CH: CHIRP threshold (dB); OS: Compared stimulus amplitude.

VEMP-CHIRP, LS CE-CHIRP, 360-720 Hz CE-CHIRP, 500 Hz LS CE-CHIRP.

Most of the literature studies were conducted on healthy participants. The mean age of participants was 31.54 years in these studies. The response rate range was 85%-100% with CHIRP stimuli. In response to the CHIRP stimulus, the average P1 latency was 10.83 milliseconds (ms), the average N1 latency was 18.95 ms, and the average P1-N1 amplitude was 92.20 microvolts (µV) in the cVEMP test. cVEMP responses are affected by the stability of SCM muscle contraction. False negative responses may occur in patients unable to maintain SCM muscle contraction. Amplitude normalization is the scaling of the wave amplitude according to the SCM contraction. Thus, the effect of SCM contractile capacity on VEMP responses is reduced. In addition, amplitude normalization in cVEMP reduces intersubject variability. Mat et al., Aydın et al., Aydın and Erbek reported normalized amplitude values in the literature. The mean of normalized amplitude values was 1.42 µV with CHIRP stimuli.[16-18]

CHIRP stimuli were compared with 500 Hz tone burst and tone pip in the literature. In most studies, shorter P1 and N1 latency was obtained with the CHIRP stimulus in the cVEMP test.[15-21] Besides, Walther and Cebulla state that they found longer P1 and N1 latency with CHIRP stimulus.[22]

Wang et al., Moinudeen et al., Walther and Cebulla state that CHIRP stimuli produce higher amplitude values in the cVEMP test.[15,22,23] Besides, Özgür et al. and Murofushi et al. reported lower amplitude values with CHIRP stimuli.[19,20] Ocal et al., Aydın and Erbek stated that there was no statistically significant difference between CHIRP and tone burst stimuli findings.[18,21] There is only one study in the literature reporting cVEMP threshold values.[18] They reported statistically significant lower cVEMP threshold values with CHIRP stimulus in healthy participants.

Differences in the findings of the studies may be due to the difference in stimulus and recording parameters used, the age range of samples, sample sizes, SCM muscle contraction capacity of participants, and the tuning effect of the otolithic organs.

OVEMPS RESULTS WITH CHIRP STIMULI IN HEALTHY INDIVIDUALS

There are 6 oVEMP studies in which CHIRP stimulus is evaluated in the literature (Table 2). The first study in which the CHIRP stimulus was evaluated in the oVEMP test was conducted by Walther and Cebulla in 2016.[22] Several types of CHIRP have been used in these studies such as 250-1,000 Hz CW-VEMP-CHIRP, 500 Hz CE-CHIRP, 500 Hz LS CE-CHIRP, 10-10,000 Hz CHIRP. The mean age of participants was 38.47 years in the literature. The response rate range was 90%-100% with CHIRP stimuli. The observation of higher response rates with CHIRP stimulus supports the advantage of CHIRP stimulus in the VEMP test. In response to the CHIRP stimulus, the average N1 latency was 6.61 ms, the average P1 latency was 11.82 ms, and the average N1-P1 amplitude was 11.33 µV in the oVEMP test.

CHIRP stimuli were compared with a 500 Hz tone burst. Bas et al., Karaçaylı et al., Mat et al, Aydın et al., Aydın and Erbek reported shorter N1 and P1 latencies with CHIRP stimulus.[16-18,24,25] On the other hand, Walther and Cebulla indicated that there was no statistically significant difference in N1 and P1 latencies.[22] In all studies, higher N1-P1 wave amplitude values were reported in oVEMP. There is only one study in the literature reporting oVEMP threshold values.[18] They reported statistically significant lower oVEMP threshold values with CHIRP stimulus in healthy participants.

VEMPS RESULTS WITH CHIRP STIMULI IN PATIENTS

VEMP test is valuable to assess vestibular disorders such as superior semicircular canal dehiscence syndrome, vestibular neuritis, Meniere's disease/endolymphatic hydrops, and vestibular schwannoma. Vestibular system pathologies affect VEMP findings. In vestibular disorders, VEMP response rates are lower than in healthy individuals. However, it is questionable whether the lower response rates are due to pathology, or or it is a false negative response. Therefore, stimulus studies in the VEMP test should also be performed on patients. In the literature, there are very few studies of VEMP in which the CHIRP

TABLE 2: Ocular vestibular evoked myogenic potentials studies in which CHIRP stimulus is evaluated.[21]

		Publication year	Number of healthy controls	Number of patients	Mean age of participants	CHIRP type	Compared stimulus	Stimulus intensity level (dB)	Response rate of CHIRP (%)	Response rate of compared stimulus (%)	CHIRP N1 latency (ms)	Compared stimulus N1 latency (ms)	CHIRP P1 latency (ms)	Compared stimulus P1 latency (ms)	CHIRP amplitude (µV)	Compared stimulus amplitude (µV)	CHIRP threshold CH (dB)	Compared stimulus threshold OS (dB)
Walther and Cebulla[22]		2016	10	-	37.5	250-1,000 Hz CW-VEMP-CHIRP	500 Hz TB	100	90	90	-	-	-	-	3.5	2.9	-	-
Karaçaylı et al.[25]		2020	60	-	25.8	500 Hz CE-CHIRP	500 Hz TB	100	100	100	5.1	10.63	9.81	15.51	16.67	12.27	-	-
Bas et al.[24]		2020	85	-	36.9	10-10,000 Hz CHIRP	TB	105	98.8	94.1	5.99	10.06	11.22	15.01	10.92	7.18	-	-
Mat et al.[15]		2021	21	-	36.4	500 Hz CE-CHIRP	500 Hz TB	100	100	100	-	-	-	-	-	-	-	-
Aydın et al.[17]		2022	56	-	34.6	250-10,900 Hz CHIRP	500 Hz TB	105	96.4	78.5	7.59	11.05	13.34	16.53	3.96	3.19	-	-
Aydın and Erbek[18]	Controls		54		40.9	500 Hz LS CE-CHIRP	500 Hz TB	100	99	99	7.76	10.65	12.92	16.51	21.61	15.15	86.48	91.43
	Patients			50	53.3			100	93.5	91.5	8.2	11.28	13.65	16.65	14.63	11.59	90.18	93.72

CHIRP: Claus Elberling Compressed high-intensity radar pulse; VEMP: Vestibular evoked myogenic potential; CE-CHIRP: Claus Elberling CHIRP; LS: Level-specific; CH: CHIRP threshold (dB); OS: Compared stmulus threshold (dB) stimulus is evaluated. Murofushi et al. evaluated cVEMP with CHIRP stimuli in 16 patients (7 with Meniere's disease/endolymphatic hydrops, 7 with vestibular migraine, and with 2 recurrent peripheral vestibulopathy).[20] Aydın and Erbek assessed cVEMP and oVEMP with CHIRP stimuli in 50 patients (24 with Meniere's disease, 14 with benign paroxysmal positional vertigo, 12 with vestibular neuritis) in addition to 54 controls.[18] The mean age of the patients in these studies was 48.1 years. LS CE-CHIRP and Narrowband LS CE-CHIRP stimuli were evaluated in these studies.

The response rate range was %81.2-%96 with CHIRP stimuli in cVEMP. In cVEMP response to the CHIRP stimuli, the average P1 latency was 13.33 ms, the average N1 latency was 22.24 ms, and the average normalized wave amplitude was 1.12 µV in patients.

In oVEMP response to CHIRP stimulus, Aydın and Erbek reported the average N1 latency was 8.2 ms, the average P1 latency was 13.65 ms, and the average P1-N1 amplitude was 14.63 µV, and the average threshold values was 90.18 dB in patients.[18]

There is only one study in the literature reporting VEMP threshold values in patients.[18] They reported statistically significant lower VEMP threshold values with CHIRP stimulus in both healthy individuals and patients.

In addition, the delay of higher frequency presentation in up-CHIRP stimuli was reflected as the delay of VEMP responses. Prolongation of latencies in Meniere's disease/endolymphatic hydrops indicates higher frequency tuning in these patients. Therefore, prolongation of latencies could support the diagnosis of Meniere's disease/endolymphatic hydrops.[21] Administration of VEMP with CHIRP stimulus should be considered in Meniere's disease/endolymphatic hydrops patients.

CONCLUSION

In conclusion, VEMP responses are influenced by a combination of factors including tuning effects of the otolith organs, middle ear transmission, and stimulus parameters. Recently, CHIRP has been employed in VEMP testing, albeit with a limited number of studies primarily conducted on healthy subjects, using various CHIRP stimuli types. While many studies report enhanced VEMP responses with CHIRP stimulation in terms of higher amplitudes, shorter latencies, and increased response rates, conflicting findings exist. This review integrates findings from studies examining CHIRP stimuli in both cVEMP and oVEMP tests, suggesting CHIRP as an effective stimulus for VEMP testing. Future investigations should explore different types of CHIRP stimuli in both cVEMP and oVEMP tests, utilizing larger sample sizes and diverse patient cohorts.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Berna Deniz Kuntman;* ***Design:*** *Berna Deniz Kuntman;* ***Control/Supervision:*** *Berna Deniz Kuntman;* ***Analysis and/or Interpretation:*** *Berna Deniz Kuntman, Anı Parabakan Polat;* ***Literature Review:*** *Berna Deniz Kuntman, Anı Parabakan Polat;* ***Writing the Article:*** *Berna Deniz Kuntman, Anı Parabakan Polat;* ***Critical Review:*** *Berna Deniz Kuntman, Anı Parabakan Polat.*

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