

## The effect of preterm birth on vestibular evoked myogenic potentials in children

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### Abstract

**Background:** Preterm birth is a significant global health problem with serious short- and long-term consequences. This study examined the long term effects of preterm birth on vestibular evoked myogenic potentials (VEMPs) among preschool-aged children.

**Methods:** Thirty-one children with preterm and 20 children with term birth histories aged 5.5 to 6.5 years were studied. Each child underwent VEMPs testing using a 500 Hz tone-burst stimulus with a 95 dB nHL (normal hearing level) intensity level.

**Results:** The mean peak latencies of the p13 and n23 waves in the very preterm group were significantly longer than for the full-term group ( $p \leq 0.041$ ). There was a significant difference between very and mildly preterm children in the latency of peak p13 ( $p = 0.003$ ). No significant differences existed between groups for p13-n23 amplitude and the interaural amplitude difference ratio. The tested ear and gender did not affect the results of the test.

**Conclusion:** Prolonged VEMPs in very preterm children may reflect neurodevelopmental impairment and incomplete maturity of the vestibulospinal tract (sacculocollic reflex pathway), especially myelination. VEMPs is a non-invasive technique for investigating the vestibular function in young children, and considered to be an appropriate tool for evaluating vestibular impairments at the low brainstem level. It can be used in follow-ups of the long-term effects of preterm birth on the vestibular system.

**Keywords:** Vestibular evoked myogenic potential, Vestibulospinal tract, Sacculocollic reflex, Preterm birth, Term birth.

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### Introduction

Early interaction with a marginally inappropriate extra-uterine environment in pre-term infants could play a crucial role in short- and long-term sequelae. Results from previous studies confirm the presence of high rates of neurodevelopmental impairment among preschool children with pre-term birth history that span neuromotor functioning, cognition, language, and emotional/behavioral adjustment (1). The aver-

age rate of preterm birth is 9.6% World-wide (2). In the last two decades, the rate of survival after preterm birth, especially in socio-economically developed countries, has significantly increased (3). This is mainly the result of improvements in neonatal intensive care. Studies investigating brain structural development in prematurely born group consistently show structural alterations in both cortical and sub-cortical structures at birth and, considerably,

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throughout childhood and adolescence (4).

Vestibular evoked myogenic potential (VEMP) is a short-latency response of the sternocleidomastoid muscle following high level of acoustic stimulation. It is a manifestation of the vestibulocollic reflex, originated in the saccular macula, which moves through the vestibular nerve and nucleus, the vestibulospinal tract, on to the motor neurons of the sternocleidomastoid muscle (5). VEMPs are used for diagnoses ranging from otologic disorders to neuropathies and brainstem lesions (6). Delayed reflex is typically seen in central pathology. If there is no conductive hearing loss, the lesions of the end-organs, primary afferents, and the nerve root entry zone lead to absence of response (5).

Although studies on VEMPs in preterm groups are rare in the literature, the available results of studies on preterm infants consistently have shown that they are at risk of disability related to maturation of the vestibulocollic reflex (7-9). The vestibular system is important to motor development; vestibular dysfunction may lead to delayed postural control and locomotor development at later ages (10). Children with histories of preterm birth are at greater risk for motor disabilities and poor postural control than those with normal deliveries (11, 12). This group should be followed closely for vestibular deficiency-related complications. The present study investigated the long term effects of preterm birth on the vestibulocollic reflex pathway.

### Methods

This comparative-analytic study was performed on 31 children with histories of preterm birth (18 males, 13 females) and 20 with term births as controls (9 males, 11 females). The subjects were 5.5 to 6.5 yr of age and enrolled in the audiology clinic at school of rehabilitation between February and July of 2013. Children with preterm history were divided into very preterm (VP; less than 32 wk) and mildly preterm (MP; 32 to 37 wk) groups. The VP group comprised 10 children (6 males, 4 females) and

the MP group 21 children (12 males, 9 females). The mean gestational age for the VP, MP, and control groups were  $30.6 \pm 0.94$  (28-31 wk),  $34.9 \pm 1.28$  (33-37 wk), and  $39.6 \pm 0.74$  (38-41 wk), respectively. The exclusion criteria for all groups were a history of congenital abnormalities, ototoxic drug use, recurrent ear infections, previous ear surgery, high fever, head trauma, mental retardation, and psychological problems (based on parental report). Parental approval, good general health of the child, absence of abnormalities of the external and middle ear, normal peripheral hearing (tested by conventional pure-tone audiometry and normal results for tympanometry) were considered as inclusion criteria for all children. The subjects were selected through a review of their medical records for the past 5.5 to 6.5 yr.

An ICS Charter EP device was used to record surface electromyographic activity of the SCM muscle. The active electrodes were attached to the upper half of the bilateral SCM muscles; a reference electrode was attached to the suprasternal notch and a ground electrode to the forehead. To elicit the desired response from each ear, the child was trained to rotate his or her head toward the contralateral side and keep his or her head in this position for several seconds (13). The children were awake and none sedated during the course of the test. Short tone bursts (95 dB nHL, 500 Hz each, rise-and-fall time = 2 ms, plateau time = 0 ms) were delivered monaurally using an ER-3A insert receiver. The stimulation rate was 5.1 Hz with the analysis time of 100 ms. The 150 responses to stimuli were then averaged, and their band-pass filtered (10-1500 Hz) and amplified (5000 $\times$ ) (14). Measurements were repeated twice to check test wave reproducibility.

Normal distribution of data was assessed by the One-Sample Kolmogorov-Smirnov test. The One-way ANOVA Post-Hoc LSD *c*test was used to compare the results. For statistical analysis, the data were presented as a mean  $\pm$  (standard deviation (SD)). All statistical analyses were done using SPSS

Statistics 18.0 at significance level of 0.05. This study was approved by the ethics committee of Tehran University of Medical Sciences.

## Results

No statistically significant differences were observed between results of the both ears ( $p \geq 0.215$ ). Biphasic waveforms for VEMPs were obtained for all children in the three groups. The mean latencies of the p13 and n23 waves for all groups are compared in Fig. 1.

According to the one-way ANOVA statistical test the difference between three groups was significant in p13 latency ( $F=5.68$ ,  $p=0.005$ ), but not significant for n23 latency ( $F=2.33$ ,  $p=0.10$ ), p13-n23 amplitude ( $F=0.12$ ,  $p=0.88$ ) and interaural amplitude difference ratios ( $F=0.49$ ,  $p=0.60$ ). Results from precise analysis by ANOVA Post-Hoc LSD test are shown in Table 1.

Significant differences were observed in the latency of the p13 ( $p=0.002$ ) and n23 ( $p=0.041$ ) waves between the VP group and control group. Fig. 2 shows sample responses recorded from the right ear in one VP and one normal child. A significantly prolonged p13 latency was observed in the VP group over the MP group ( $p=0.003$ ). Moreover there was no significant difference between the MP and control groups

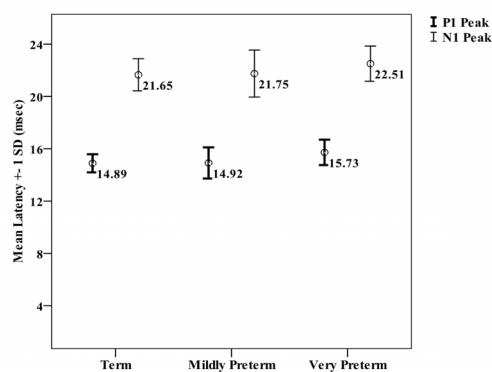


Fig. 1. Comparison of the mean p13 and n23 latency between three groups.

for all test parameters ( $p \geq 0.773$ ).

There was no significant difference between the three groups in p13-n23 amplitude ( $p \geq 0.627$ ) and interaural amplitude difference ratios ( $p \geq 0.348$ ). Sex had no effect on the results ( $p \geq 0.103$ ). No significant differences were observed between the left and right ears for each group.

## Discussion

Although, no similar study has been published on preschool aged children with preterm birth history, previous studies on term children reported non-significant differences between the right and left ears (15-17). It appears that maturation occurs similarly for ears on both sides. This reflective response generates from the lower brainstem and laterality has little effect on this potential.

Table 1. Comparison of the VEMPs in three groups

	Normal Children (N)	Mildly preterm (MP)	Very preterm (VP)	Groups	p
N (ears)	40	42	20		
P13 Latency (ms)	14.89 (0.69)	14.92 (1.19)	15.73 (1.02)	N,MP	0.906
				N,VP	0.002
				MP,VP	0.003
n23 Latency (ms)	21.65 (1.22)	21.75 (1.79)	22.51 (1.41)	N,MP	0.773
				N,VP	0.041
				MP,VP	0.068
p13-n23 amplitude ( $\mu V$ )	162.13 (122.9)	160.00 (84.46)	139.77 (79.57)	N,MP	0.924
				N,VP	0.627
				MP,VP	0.681
Interaural amplitude difference ratio	18.82 (9.69)	19.05 (17.24)	24.59 (13.49)	N,MP	0.943
				N,VP	0.348
				MP,VP	0.377

Data are expressed as mean (SD).

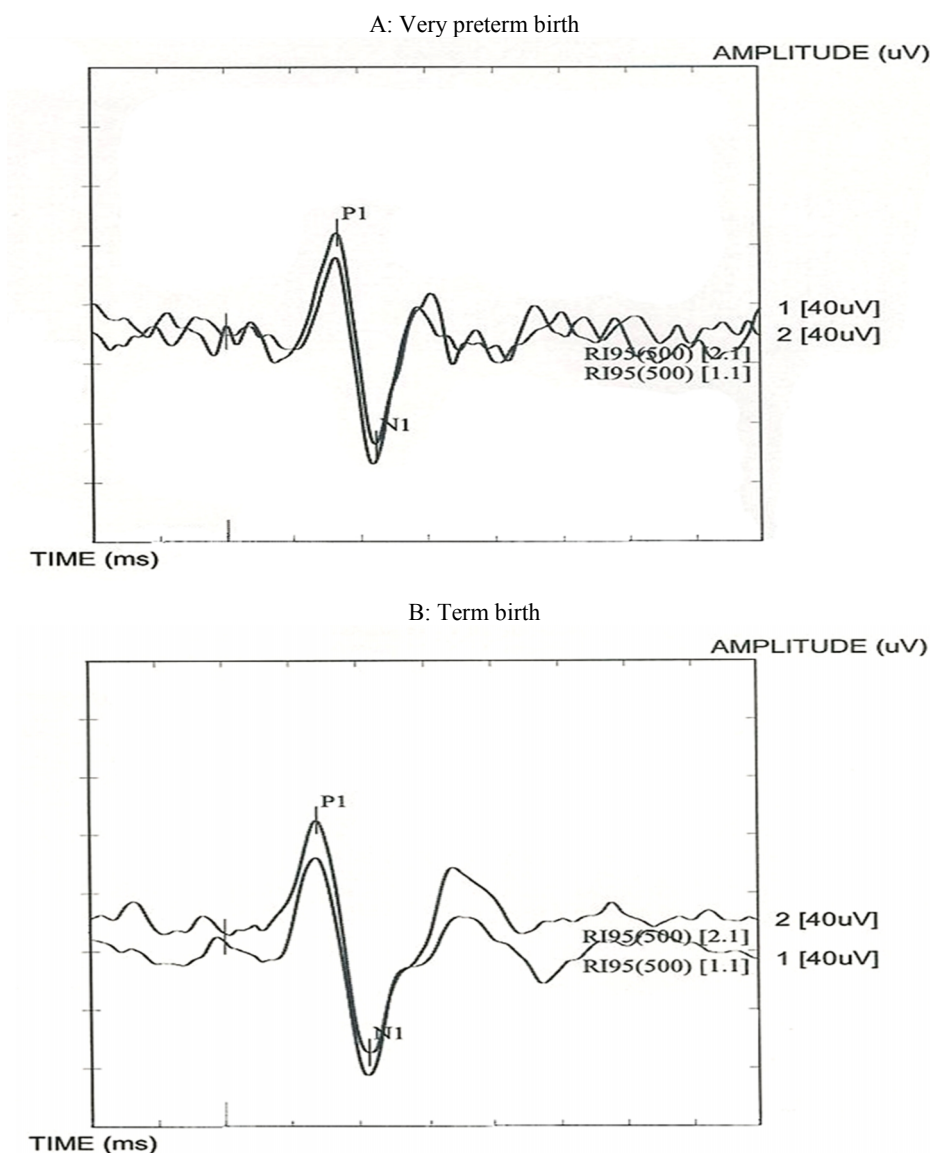


Fig. 2. VEMPs result of very preterm child (A) versus normal child (B).

The VP group showed significantly longer p13 and n23 latencies than the control group. Studies on preterm infants have also shown abnormal VEMPs results. Ecevit et al. (7) studied 17 late preterm infants (mean gestational age:  $35.11 \text{ wk} \pm 0.78$ ) at 8 wk postnatal and found that the latencies of p13 and n23 in preterm infants were significantly longer than for term infants. Erbek et al. (8) studied 50 newborns with a mean gestational age of  $31.7 \pm 2.7 \text{ wk}$  (range=26-36 wk). The results showed a significant difference between abnormal VEMPs rates for preterm and full term infants. Wang et al. (9) studied 27 low-risk preterm neonates and found that mean latency of peaks p13

and n23 in the preterm group were significantly longer than those in the full-term group. It has been reported that conditions affecting the vestibulospinal tract result VEMPs delay and that vestibule disorders frequently led to lack of response (18). Imaging studies confirmed structural alterations in cortical and sub-cortical structures at birth, and in childhood and adolescence in the preterm group (4). In other hand, previous studies have shown that the auditory brainstem response (ABR) was affected by preterm birth in infancy and at preschool age. For instance, Hasani et al. (19) studied 30 children with histories of preterm birth with 4-6 yr of age. Significant

differences in the ABR test results were observed for the inter-peak intervals of the I-III and III-V waves and the absolute latency of the III wave. Overall, prolonged VEMPs in VP children may reflect incomplete maturation (especially myelination) and deficits in their vestibulospinal tract.

In the present study, no significant difference was found between the MP and control groups for wave latency of VEMPs. In contrast, Ecevit et al. (7) reported that wave latency for VEMPs in late preterm infants (34-36 wk) was significantly longer than those with full term. This condition may relate to the delay in maturation of the sacculocollic pathways in the MP group in infancy. In other hand, the VP was significantly different from the MP group for p13 latency. Previous studies have shown that the risk of mortality, morbidity, and neurodevelopmental impairment was tightly linked to gestational age and reached the highest rate for infants born at less than 32 wk (very preterm) (2, 20). Consequently, increased gestational age (GA) in children born at GA > 32 wk gestation showed less long-term sequelae than children with GA < 32 wk.

The p13-n23 amplitude did not differ between the three groups of children in this study. This is consistent with the findings of Wang et al. (9) on preterm and term infants; these groups showed no significant differences in the raw and corrected p13-n23 amplitudes. VEMPs amplitude is dependent upon sound intensity and constriction of the SCM muscle (21). Accordingly, since there are large variability in response amplitude, especially for the very young, fewer studies have considered it. The interaural amplitude difference ratio is the more informative parameter for investigating unilateral vestibular disorders (14). In the present study, the interaural amplitude difference ratio showed no significant difference between groups. These findings support the possibility of a symmetrical function of the vestibular system for both ears.

No significant difference was observed

between the two genders for the test parameters. Previous studies have also reported no effect for gender on VEMPs responses (15, 22, 23). These findings could be a consequence of the elicitation of these reflecting responses from the lower brainstem (24).

Findings of the present study revealed the positive effect of augmented in age on the improvement of VEMPs results. Thus, in comparison with Wang et al. (9) study which VEMPs was not appeared in 74% of preterm neonates, in the present study, VEMPs was obtained in all children of the studied groups. Although, in the present study, abnormal VEMPs results were still observed, especially in the VP group. The early exposure to an extra-uterine environment for the VP group could exposed the neurodevelopmental process of these infants to physiological, psychological, and environmental hazards (25). It can be concluded that deficits in the central vestibular pathway could be related to incomplete myelinization of the neural pathways and the consequent delay in nerve conduction can leads to abnormalities such as delayed p13 and n23 waves in VEMPs.

Improvements in hygiene and reductions in the birth rate have decreased the incidence of preterm birth in Iran and, consequently, decreased the pool of these children with a history of preterm birth (especially very preterm). Future studies should expand access to the population sample of preterm children in different regions so that longitudinal studies can be designed to obtain more precise information about the effect of preterm birth on vestibular evoked myogenic potentials and the neurodevelopmental process on improvements in this response. Moreover, behavioral assessments of the vestibular system, especially on static balance skills, and electrophysiological tests can clarify the role of structural disabilities in balance and provide subtle information for counseling and planning useful treatment programs.



## Conclusion

The significant finding of the current study is the prolonged latency of p13 and n23 waves in the VEMPs in children with very preterm birth histories compared with those with histories of mildly preterm and full term births. Possibly, the delay in and deficit of the neural pathway of the vestibulocollic reflex and inadequate neural synchronization were the main causes for the difference. The results of this study provide information about effects of preterm birth for both specialists and parents. Since the VEMPs test evaluates the function of a part of the vestibular system, the probable effects of preterm birth on other aspects of the vestibular and balance systems should be studied. Other area of future research should explore the usage of VEMPs testing on performance of vestibulocollic reflex among children with preterm birth at the preschool age.

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## Conflict of interest

The authors declare that they have no competing interests.

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