

## Static balance function in children with a history of preterm birth

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### Abstract

**Background:** The incomplete maturation of brain in preterm children results in long-term neurodevelopmental impairment. This study aimed to investigate the static balance function in children with a history of preterm birth.

**Methods:** Participants were 31 preterm children including 21 moderately preterm (MPT), 10 very preterm (VPT), and 20 term children aged 5.5 and 6.5 years. The cervical vestibular-evoked myogenic potential (cVEMP) test and four static balance subscales of BOT-2 were performed.

**Results:** The VPT children showed a significant increase in P1 and N1 wave latencies in cVEMP test compared to those in the term children ( $p=0.041$ ). Mean scores in the four static balance subscales of BOT-2 were significantly lower in the preterm children compared to those in the term children ( $p=0.025$ ). The P1 wave latency ( $p=0.003$ ) and mean score of standing on a balance beam with open eyes ( $p=0.039$ ) were significantly lower in the VPT children compared to those in the MPT children. A significant correlation was observed between the mean score in exercise 4 (standing on one leg on a balance beam with closed eyes) of static balance subscales of BOT-2 and P1 ( $r=-0.267$ ,  $p=0.036$ ) and N1 ( $r=-0.304$ ,  $p=0.016$ ) wave latencies of cVEMP.

**Conclusion:** The longer latency of cVEMP waves along with a poor performance of children with a history of preterm birth suggests a possible defect in central vestibular pathway.

**Keywords:** Preterm Birth, Static Balance, Preschool Children, Vestibular Evoked Myogenic Potentials.

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### Introduction

A myriad of genetic, environmental, and social factors influence the growth and development of individuals during fetal and neonatal life (1).

In addition, the neonate initiates extra-uterine life earlier than anticipated; therefore, experiences various kinds of physiological, psychological, and environmental hazards (2).

Moreover, the disruption of developmental process leads to short term, long term, and even permanent consequences. Myelination of nervous system in the fetus be-

gins from the caudal end of the neural tube and progresses toward the cephalic end (3). Therefore, the consequences of preterm birth are expected to be most severe in the central nervous system. Accordingly, imaging studies have revealed cortical and sub-cortical disorders during infancy, childhood, and adolescence among such individuals (4), which is in line with their neural growth. This group has been previously shown to suffer from various disorders pertaining to neural growth and development; cognitive, motor, and linguistic as well as long-term disorders such as cerebral palsy,

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learning disorder, and antisocial behavior are also prevalent among them (5,6).

In addition, premature infants are more prone to motor disorders and poor postural performance during childhood compared to their peers born at term (7,8). A meta-analysis of different aspects of motor development in preterm infants from birth until adolescence was conducted using the following three practical and valid tests: BSID-II (Bayley Scales of Infant Development version II), MABC (Movement Assessment Battery for Children), and BOTMP (Bruininks-Oseretsky Test of Motor Proficiency). Significant disorders of motor skills in very preterm infants and those with low birth weight were reported in this study. Moreover, such disorders continued until their teen years. In addition, the balance skills of preterm children were found to be highly defective (9). Balance is defined as a state of action and reaction between two or more parts or organs of the body. Static balance as required for normal standing is the ability to maintain the body equilibrium in some fixed posture (10).

The cervical vestibular-evoked myogenic potential (cVEMP) test is a simple, tolerable, and noninvasive test for assessing the vestibular function in infants and children. This test assesses the inhibitory response of the sternocleidomastoid (SCM) muscle to high-intensity sound stimuli. The cVEMP test provides worthwhile information on saccular integrity and neural pathways of sacculocollic reflex including inferior vestibular nerve, lateral vestibular nuclei, medial vestibulospinal tract, and motor neurons of the SCM muscle. Normal cVEMP response consists of biphasic waveforms (positive and negative). These components are labeled as p1 and n1 or p13 and n23 waves. The absence of response typically results from lesions of the end organs if there is no conductive hearing loss; and pathologies in the central neural pathways lead to delayed reflex (11). Studies that employed cVEMP test on preterm groups suggest an increased probability of disorders related to sacculocollic reflex path-

way; also, a decrease in response and a significant increase in the latency of the waves were observed in the preterm groups compared to the term ones (12-15). On the other hand, the use of behavioral tests besides this electrophysiological evaluation can provide further information on the probable structural defects that affect balance skills.

Assessing the long-term effects of preterm birth is of high significance. In this context, the American Psychological Association (APA) has emphasized the need to conduct extensive studies on the consequences of disturbed neural and behavioral development in preterm children (16). Given the important role of the vestibular system in motor development, defects in vestibular functions during infancy have a potential negative influence on other motor skills, vision growth, postural control, motor coordination, and sensory integration (17). Previous studies suggest defects in the maturation of sacculocollic reflex in preterm infants. Moreover, disorders related to motor development are observed even in adolescents with a history of preterm birth (9). Considering the importance of identifying the potential difficulties children might experience prior to the start of the elementary school, we aimed to investigate the static balance function in preschool children with a history of preterm compared to full-term birth using behavioral and electrophysiological tests.

## Methods

### *Participants*

This study included 31 children with a history of preterm birth. Based on the World Health Organization (WHO) that classified preterm infants as being moderate or late (32 to <37 gestational weeks), very (28 to <32 weeks) and extremely (less than 28 weeks) preterm (18). The preterm children were divided into two groups: 1) Moderately preterm (MPT), with a mean  $\pm$  SD gestational age of  $34.9 \pm 1.28$  weeks (range 32–37 weeks) including 12 boys and 9 girls; 2) very preterm (VPT), with a mean

$\pm$  SD gestational age of  $30.60 \pm 0.94$  weeks (range 28–31 weeks) including six boys and four girls. The control group included 20 children with a history of full-term birth including 9 boys and 11 girls; all the children aged 5.5 - 6.5 years. It should be specified that the incidence of very preterm birth is low, as the VPT infants constitute only 10.4% of preterm infants (18). On the other hand, although improvements in medical care have led to improved survival rate of VPT infants, these infants are still more prone to mortality risk (19). Therefore, accessibility to this group was very difficult and the number of sample in this group was lower than that of the other groups.

Normal peripheral hearing, good general health and absence of history of ototoxic drug use, recurrent ear infection, high fever, head trauma, ear or brain surgery and psychological problems were the inclusion criteria in the three groups. Preterm children were selected by reviewing medical records of children of 5.5–6.5 years of age. The age-matched control group was selected by reviewing the medical records of term births children with gestational age of more than 37 weeks from 5.5 to 6.5 years ago. All children were selected using simple random sampling method. On the day of the evaluation, personal meetings were conducted with parents, their consent was obtained, and the case history form was completed. Children were also subjected to basic audiometry tests including immittance audiometry (tympanometry and acoustic reflex measurements) using GSI TympanoStar (Grason-stadler Company), GSI TympanoStar and pure tone audiometry tests using GSI 61, a two-channel clinical audiometer (Grason-stadler Company). In immittance audiometry tests, normal tympanogram (type A<sub>n</sub>) and the record of acoustic reflexes were considered to rule out any type of conduction disorder (20). Moreover, air and bone conduction thresholds from 0 to 15 dB were considered as normal peripheral sensitivity (21). This study was approved by The Ethics Committee of Iran University of Medical Sciences.

### Measures

**cVEMP test:** The cVEMP test was conducted using ICS Charter EP (GN Otometrics Company). A single-channel recording of the response was made using non-inverting, inverting and ground electrodes placed on the upper half of the SCM muscle, the upper edge of the sternum and forehead, respectively. The stimulus included 500-Hz tone-bursts at 95 dB nHL intensity, with rise-fall and plateau durations of 2-0-2 c/s and rarefaction polarity. The stimulus was presented to each ear using ER-3A insert earphones. A 10- to 1500-Hz band pass filter, 100-ms time window, and stimulation rate of 5.1/s were employed; the responses were amplified 5000 times, and 150 sweeps were averaged for each test (22). To record the cVEMP, the child was seated on a chair with his/her back against a back support and the head free to move. Then, the place of the electrodes was cleaned with a special abrasive gel. To elicit responses, the child was asked to turn his/her head against the direction of the stimulated ear. Based on the feedback method for monitoring the SCM contraction by Sphygmomanometer, the degree of head rotation was controlled by the investigator as the head flexed approximately 30 degrees forward and rotated approximately 30 degrees to the contralateral side of the stimulated ear. The child was made to hold the cuff, which was inflated to a standard pressure of 20 mmHg to obtain a cushion to push against between the contralateral hand and the jaw. Then the child pushed with his/her head against the hand-held cuff (by turning the head toward the cuff) to generate a contraction in the SCM muscle ipsilateral to the stimulated ear; and the child was trained to fix it on 40 mmHg (23). The latency of the cVEMP waves was assessed as the interval of p1 and n1 apex from the baseline, and the amplitude of the waves was assessed as the voltage between two positive and negative ends of the p1–n1 complex (22). The test was conducted without the use of sedatives in subjects who remained awake. About 1–2 minutes of re-

laxation was offered between consecutive wave recordings. Wave reproducibility was checked by recording each wave twice.

#### *Assessment of the Static Balance Performance*

The static balance performance of children was assessed using four static balance subtest of BOT-2. Exercises 1 and 2 involved the child standing on the preferred leg on a straight line drawn on the ground with open and closed eyes, respectively, with both hands on the waist and the free leg bent for 10 seconds. In each exercise, if the free leg touched the ground, and formed an angle wider than 45 degrees, it was lowered, and hooked behind the standing foot, or the standing leg was moved; and then the test had to be stopped before the 10-second duration. In this instance, the recorded time would reflect the time the child had managed to maintain balance. Exercises 3 and 4 involved the child standing on the preferred leg on a straight line drawn in the middle of a balance beam with open and closed eyes, respectively, with hands around his/her waist for a duration of 10 seconds. The scoring method was similar to that of the previous stages. The balance subtest of the BOT-2 test was conducted with the children wearing comfortable shoes and in a room without any distracting objects. Second and third chances were provided for children who failed in the first try in any of the stages, and the best result was recorded.

Scoring was done separately for each stage (24).

#### *Data Analysis*

Kolmogorov–Smirnov test was employed to determine the normal distribution of data. The results of cVEMP test were compared between the three groups using one-way ANOVA test. The F values, p values and estimations of effect size (partial  $\eta^2$ ) of the confidence intervals (CI) are reported. The mean scores of children in the behavioral assessment of static balance were analyzed using Kruskal–Wallis test. The association between cVEMP wave latencies and the mean scores of children in the behavioral balance test was examined using Spearman correlation test. All statistical analyses were done using SPSS version 18.0, with the level of significance set at  $p < 0.05$ .

### **Results**

#### *cVEMP Test*

The cVEMP responses, characterized by biphasic waves, were recorded for all the study participants. A significant difference was observed between the three groups in the mean latency of P1 wave ( $p = 0.004$ ). This difference results from the differences between the VPT and the control groups ( $p = 0.002$ ) and also between the MPT and the VPT groups ( $p = 0.003$ ). Moreover, the VPT children showed a significant increase in the N1 wave latency compared to the term children ( $p = 0.041$ ). Table 1 displays

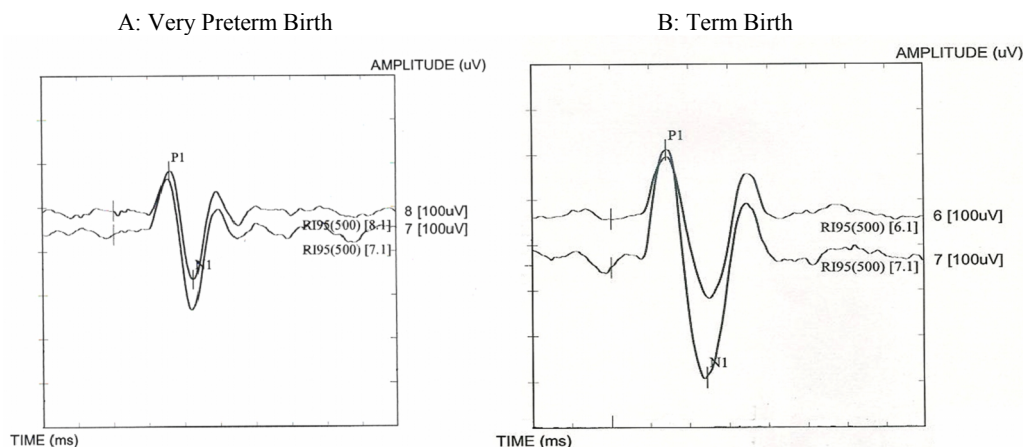


Fig. 1. P1 and N1 Waves of the cVEMP test from a Very Preterm Child (A) and a Term Child (B)

Table 1. Comparison of the cVEMP Results between the Three groups

VEMP	Term (n= 40 ears)	MPT (n= 42ears)	VPT (n= 20ears)	Statistical Results					
	Mean (SD)	Mean (SD)	Mean (SD)	F	P (total)	Partial $\eta^2$	95% CI (LB, HB)	Groups	p
P1 Latency (ms)	14.89 (0.69)	14.92 (1.19)	15.73 (1.02)	5.758	0.004	0.104	(0.012, 0.215)	T, MPT T, VPT MPT, VPT	0.906 0.002 0.003
N1 Latency (ms)	21.65 (1.22)	21.75 (1.79)	22.51 (1.41)	2.36	0.099	0.0461	(0.000, 0.135)	T, MPT T, VPT MPT, VPT	0.773 0.041 0.068
P1-N1 Amplitude ( $\mu$ V)	162.13 (122.9)	160.00 (84.46)	139.77 (79.57)	0.365	0.695	0.007	(0.000, 0.055 )	T, MPT T, VPT MPT, VPT	0.924 0.627 0.681
Interaural ampli- tude difference ratio	18.82 (9.69)	19.05 (17.24)	24.59 (13.49)	1.878	0.158	0.037	(0.000, 0.12)	T, MPT T, VPT MPT, VPT	0.943 0.348 0.377
Threshold	76.12 (4.99)	77.85 (7.50)	79.25 (4.94)	1.87	0.159	0.037	(0.000, 0.12)	T, MPT T, VPT MPT, VPT	0.305 0.058 0.494

CI: Confidence interval, cVEMP: Cervical vestibular evoked myogenic potentials, LB: Low bound of CI, HB: High bound of CI, ms: Millisecond, MPT: Moderately preterm, Partial  $\eta^2$ : Effect size estimate, SD: Standard deviation, T: term, VPT: Very preterm,  $\mu$ V: Micro volt

Table 2. Comparison of the Balance Subtest of BOT-2 test results between the Three Groups

Static balance exercises	Term (n= 40 ears)		MPT (n= 42 ears)		VPT (n= 20 ears)		P (total)	Groups	p
	Mean	SD	Mean	SD	Mean	SD			
Standing on one leg on a straight line with eye open (per sec)	9.70	0.97	9.14	1.87	8.10	3.41	0.308	T, MPT T, VPT MPT, VPT	0.362 0.127 0.436
Standing on one leg on a straight line with eye closed (per sec)	8.70	2.25	6.19	3.01	5.70	2.94	0.004	T, MPT T, VPT MPT, VPT	0.003 0.004 0.749
Standing on one leg on a balance beam with eye open (per sec)	5.85	4.15	2.95	3.54	0.50	1.08	0.001	T, MPT T, VPT MPT, VPT	0.017 0.001 0.039
Standing on one leg on a balance beam with eye closed (per sec)	1.75	1.61	0.95	2.13	0.000	0.00	0.002	T, MPT T, VPT MPT, VPT	0.025 0.001 0.147

BOT-2: Bruininks-Oseretsky test-2, MPT: Moderately preterm, SD: Standard deviation, T: Term, VPT: Very preterm

the results of cVEMP comparisons between the groups. Comparison between the cVEMP responses of a VPT child and those of a term child is shown in Figure 1.

Furthermore, previous studies suggested that auditory-evoked potential wave latencies of the tested group, whose values deviated from the mean of the control group by more than two times standard deviation, could be considered as abnormal (3,25). Accordingly, the mean  $\pm$  SD latency of P1 wave in the control group was  $14.89 \pm 0.69$  ms in the current study, and values above 16.27 ms were considered as abnormal for the preterm group. Hence, 19.04% of MPT infants and 40% of the VPT infants, four children each in both groups, showed abnormal P1 latency.

### The Static Balance Performance

The mean scores (per sec) of children in

the three groups in each of the four static balance subtest of BOT-2 are shown in Table 2. Significant differences were observed between the three groups with respect to the mean scores in exercises 2 (standing on a straight line with closed eyes for 10 s) ( $p=0.004$ ), 3 (standing on one leg on a balance beam with open eyes) ( $p= 0.001$ ), and 4 (standing on one leg on a balance beam with eyes closed) ( $p= 0.002$ ).

### Correlation between cVEMP Findings and the Static Balance Performance

In children with preterm birth history, there was a significant correlation between mean score in exercise 4 (standing on one leg on a balance beam with closed eyes) and P1 ( $r= -0.267$ ,  $p= 0.036$ ) and N1 ( $r= -0.304$ ,  $p= 0.016$ ) wave latencies of cVEMP. This correlation was not observed in the control group ( $r \leq 0.262$ ,  $p \geq 0.1$ ).



No statistically significant difference was observed between the groups for body height and body weight ( $p \geq 0.05$ ). Furthermore, no significant correlation was observed between body height ( $r \leq 0.177$ ,  $p \geq 0.05$ ) and body weight ( $r \leq 0.202$ ,  $p \geq 0.1$ ) and the two tested parameters.

### Discussion

Children born at a gestational age of more than 26 weeks were examined in this study. Therefore, the development of the vestibular part of their inner ear could be presumed to have occurred before birth (13), which was concomitant with the cVEMP recordings for all the term and preterm children. In the current study, the prolonged wave latencies were the noticeable results of cVEMP test. Previous studies have attributed such an increase in cVEMP wave latency to the impairment of the sacculocollic neural pathways (26). Research on the preterm groups has shown that brain weight in a preterm (32 week gestation) infant is 65% of that of a term one, and the outer area of brain grooves is also limited; this underdevelopment of the brain potentially results in serious injuries (5). Imaging studies have shown that the size, volume and speed of growth of many parts of the brain including corpus callosum, ventricular system, cortex, gray matter and cerebellum are affected by preterm birth (27). During the development of the nervous system in the fetus, myelination in the brain begins during the fifth fetal month and progresses from the caudal to the cephalic parts (3). In this regard, although vestibular development is soon completed in the intra-uterine stage, the central vestibular pathways continue to grow after birth, particularly in preterm infants (13). Accordingly, the prolonged cVEMP wave latency could be a consequence of the abrupt initiation of extra-uterine life and the immaturity of central pathways. The results of this study support previous studies that investigated cVEMP in preterm infants and reported a significant increase in the latency of response waves in preterm compared with normal-born infants

(12, 13, 15). Such an increase in cVEMP wave latency in children born preterm suggests that they show symptoms of immaturity in the neural pathways not only during infancy but also during preschool years; this is particularly true of VPT children, suggesting that this immaturity has not been compensated for by growth. These defects appear to have resulted from delayed and/or defective myelination in the neural pathways of the sacculocollic reflex. However, it has to borne in mind that despite the statistically significant differences observed between the preterm and full-term children in the mean latency of p1 wave, as 19.04% of MPT and 40.0% of VPT children showed abnormal p1 latency, these results might be clinically less worthwhile; and therefore, more studies are needed for more reliable results.

In addition to the electrophysiological assessment, static balance performance was tested through behavioral exercises in this study. Four static balance subtests of BOT-2 were employed as omission or reduction of visual or somatic inputs makes balance retention more difficult, making possible the assessment of the child's performance under more challenging situations. In exercises that involved standing on one leg on a straight line with closed eyes or on a balance beam with open and closed eyes, the MPT as well as the VPT children showed significantly poorer performance compared with the control group; their mean scores in the exercises were significantly lower compared with the term children. Although none of the participants, including term children, could complete exercise 4 (standing on a balance beam with closed eyes for 10 s), the mean scores of the preterm children were significantly lower than those of the control group. These observations revealed the overall poor performance of the children who were born preterm in four static balance subtests of BOT-2. Balance is dependent on receiving visual, somatic and vestibular inputs as well as their appropriate processing in the central nervous system; therefore, a damage and/or weakness

in one of these subsystems does not pose a significant difficulty to individuals because of adaptation and/or substitution mechanisms. However, the damage of two or more of these mechanisms creates a challenge to balance the maintenance systems (28). Previous research has shown that a high percentage of preterm children experience motor developmental disorders such as balance disorders and poor postural control (7,8). The neuropathology associated with preterm birth, which has been investigated in a multitude of studies, includes defects in the development of central neural pathways, structural alterations in both cortical and subcortical structures, and low brain volume in these children (4, 6, 29, 30). Given the gestational age of the participants and the high probability of maturation of the peripheral parts of their vestibular system, their balance performance problems are possibly related to neuropathological factors, neurodevelopmental impairment and defects in neural transmission. Therefore, in the four static balance tests, balance disorders became evident in preterm children when the reception of visual and somatic inputs became difficult, as a consequence of probable defects in perceiving or processing vestibular inputs; preterm children were, therefore, significantly outperformed by the term children.

Significant differences were observed between the MPT and the VPT groups in both cVEMP and behavioral static balance subtest of BOT-2 in this study. In the cVEMP test, the latency of P1 wave was significantly longer in the VPT compared to that of the MPT group. Moreover, the mean score obtained in exercise 3 (standing on a balance beam with open eyes) of the static balance test was significantly lower in the VPT compared to that of the MPT group. These results indicate that VPT children are more prone to the long-term consequences of preterm birth compared to the MPT children. Although VPT children are more vulnerable to death, recent advancements in intensive care have increased the probability of their survival, leading to an increase

in the number of motor, cognitive, and sensory developmental disorders (5). Previous studies suggest that the risk of neurodevelopmental diseases and defects increases concomitantly with decrease in gestational age (5,12).

There were significant correlations between P1 and N1 wave latencies of cVEMP and mean scores in exercise 4 (standing on one leg on a balance beam with closed eyes) in preterm children. Such an association between electrophysiological and behavioral results was reported in another study conducted on hearing-impaired children with profound sensorineural hearing. These children, with a mean age of 6.93 years, showed a significant correlation between cVEMP response and performance in exercises 1 and 3 (31). Similar results were reported in another study (32). In general, the results of this study support the existence of probable defects in the static balance function of preterm children.

Using both electrophysiological and behavioral tests in our study enabled us to have a better judgment of the vestibular and balance functions of preterm children in tests of static balance skills. The cVEMP results of preterm children showed a significant increase in wave latencies, and these children were suspected to have impairment in the retrolabyrinthine pathway. This could indicate a delay and/or a defect in the myelination of the neural pathways of the vestibular system. On the other hand, significant differences were observed between preterm and full-term children with respect to their performance in behavioral static balance tests. The association of preterm birth with the neuropathology accompanying the delayed and/or defective maturation of the neural pathways leads to an increased probability of impairments in the neural pathways of the vestibular system.

In this study, the assessment of performance in the four static balance subtests of BOT-2, which were subtests of the BOT-2 balance test, was done based on subjective observations. Although this can be considered a limitation of this study, observations

were made by a well-instructed practitioner. In future studies, the use of more objective measurement (such as Romberg's quotient (RQ) of sway area and sway velocity) than subjective judgment can provide more precise information. On the other hand, difficulty in perusing medical records and their occasional incomprehensiveness resulted in a limited access to preterm children (particularly the VPT infants), resulting in a relatively small number of participants. A larger number of participants are, therefore, recommended for future research. Moreover, the source of the cVEMP response is probably the saccule, which is a sensory organ that detects linear accelerations and decelerations, and the cVEMP test assesses the response of linear balance (22). Therefore, the findings of this study are limited to the vestibular otolith organs, particularly the saccule; and hence, focus on other vestibular organs of the inner ear as well as the intervening mechanisms in the maintenance of balance is recommended for future research on children with a history of preterm birth. Nevertheless, one could argue that the vestibular system plays a minor role in static balance. For example, Potter and Silverman (33) concluded that the level of vestibular response was not significantly related to static standing balance; hence, findings should likely be interpreted with caution, and a further study using neurotologic measures (e.g., vestibulo-ocular reflex function and posturography) is required for the precise assessment of vestibular function and its contribution in poor performance of the children in four static balance subtests of BOT-2.

### Conclusion

The results of the balance exercises suggest that preterm children encounter problems in maintenance of static balance in challenging situations on a daily basis, which is concomitant with the observed prolonged cVEMP wave latencies. In addition, the smaller gestational age has a severe impact on test results, as the VPT children showed more severe defects in the

current study compared to the MPT children. In general, although preterm children appear to reach the main developmental milestones, not only are their growth stages delayed, but certain long-term and permanent consequences are also to be expected. Given the importance of preschool years for achieving essential developmental capabilities such as balance before entry into school, the existence of disorders such as uncompensated balance skills in preterm children is worrisome. The findings of this study emphasize the importance of early necessary screening programs for identifying at-risk children and planning the appropriate therapeutic interventions to prevent the probable consequences of preterm birth. It is allowing parents to be alerted about the potential difficulties their children might experience prior to the start of elementary school.

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