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ASSESSMENT OF SPONTANEOUS MOTOR ACTIVITY IN PREDICTING NORMAL NEUROMOTOR DEVELOPMENT IN PRETERMS

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Conventional methods of neurological assessment of newborns and infants are in daily clinical use. Since preterm newborns often have multiple risk factors for further neuromotor developmental disorders, this study aimed to determine the predictive value of spontaneous motor activity in preterms during the fidgety period for normal neurological and functional outcomes at the age of 24 months.

The study was performed as a prospective clinical study and included 80 preterm children. Observation of spontaneous motor activity was carried out according to the basic principles of Prechtl's method in the period 50–54 weeks of postmenstrual age.

All participants who showed normal fidgety movements during this period had normal neuromotor development after 24 months. Among participants with a final neurological outcome of minimal neurological dysfunction after 24 months, 73% showed abnormal fidgety movements. In the study, there were no subjects who had a normal presentation of fidgety movements and later, at the age of 24 months, were found to have neurological deficits and clinical signs suggesting the subsequent development of cerebral palsy. Preterm infants with (very) low birth weight, those born before the 30th gestational week, and those with a low Apgar score have a higher chance of neurodevelopmental deviations.

Such a high predictive value of normal general movements in period 50–54 weeks of postmenstrual age, confirms the practical importance of assessing general movements and the need for developmental follow-up for all preterm infants.

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Key words: *preterm infants, spontaneous motor activity, Prechtl's method, neurodevelopmental outcome*

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Introduction

The motor development of newborns and infants occurs completely spontaneously and directly depends on the state of the central nervous system. Conventional methods of neurological assessment of newborns and infants include neurological examination, neurokinesiological examination, quantitative assessment using scales and tests, as well as the use of supplementary diagnostic procedures such as magnetic resonance imaging, ultrasound diagnostics, and electroencephalography. All the aforementioned methods are in daily clinical use for the neurological assessment of newborns and infants (1).

These methods can provide very precise data on the damage to the central (and peripheral) nervous system, but they all share a common drawback: the inability to adequately predict neurological deficits. This fact prompted the need for a new technique and a new approach. In the early 1960s, Professor Heinz Prechtl, an Austrian neurophysiologist, attempted to create an adequate method for neurological examinations of newborns. Prechtl believed that birth could not be the starting point, but that spontaneous motor activity (SMA) must have a prenatal history. His research especially advanced with the advent of ultrasound diagnostics. The first breakthrough was discovering that complex whole-body movements occur intrauterine in the ninth and tenth weeks of postmenstrual age (PMA). Prechtl called these movements "general movements" (GMs). Their characteristic is that they are generated endogenously, are complex, and have a specific sequence of body parts involvement. Prechtl proved that GMs are present throughout the entire prenatal period and continue to exist until the 5th–

6th months post-term. Pre-term, Prechtl referred to GMs as fetal or preterm movements. At term, post-term, and up to the 6th (sometimes up to the 9th) week post-term, Prechtl called GMs "writhing" movements. During the period from the 6th to the 9th week post-term, "writhing" movements gradually disappear, and new GMs appear, which Prechtl called fidgety movements. Fidgety movements cease to manifest between the 5th and 6th month post-term. After that, voluntary and anti-gravitational movements appear and dominate (2).

Given the inconsistent and variable responses of the immature nervous system, a one-time assessment of newborns cannot provide a definitive answer regarding the presence of a particular neurological disorder. Therefore, examinations need to be repeated, which in clinical practice is called developmental monitoring. Developmental monitoring should be conducted for preterm infants, children with complications during birth, and generally for children born from high-risk pregnancies, with the aim of early diagnosis and timely treatment.

Risk factors for neuromotor developmental disorders in newborns are divided into prenatal, perinatal, and postnatal. Prenatal risk factors include all adverse morphological, circulatory, chemical, and infectious agents originating from the mother, such as anatomical and functional anomalies of the mother's reproductive system. Perinatal risk factors relate to prematurity, low birth weight of the newborn, Apgar score, multiple pregnancies, birth trauma, inadequate fetal presentation, delivery by cesarean section, etc. Postnatal risk factors are numerous, with the most common being intracranial hemorrhages, afebrile convulsions, exposure to toxic substances, and severe septic conditions (3).

Since there is a reasonable suspicion that a newborn exposed to risk factors could have a developmental deficit as a consequence, the aim of this study was to determine the predictive value of spontaneous motor activity in preterm newborns with certain risk factors, during the fidgety period, for normal neurological and functional outcomes at the age of 24 months.

Materials and Methods

The study was conducted as a prospective clinical trial as part of an investigation for the doctoral thesis (4, 5). All babies born between January 1, 2012, and December 12, 2012, at the maternity ward of the Gynecology and Obstetrics Clinic of the Clinical Centre Niš, with a gestational age ≤ 37 weeks were included in the study.

Exclusion criteria were parental refusal to participate in the study, presence of congenital anomalies, deformities, and genetic syndromes in the newborn, invalid video recordings, and failure to attend follow-up examinations (incomplete study).

During the study period, 3328 babies were born at the Gynaecology Clinic of the Clinical Centre Niš, of which 233 were preterm infants (≤ 37 weeks GA). During the study, a certain number of newborns were excluded due to fatal outcomes, transfer to other healthcare facilities (deterioration of general condition, other diseases), and failure to attend follow-up examinations (incomplete study). A total of 80 newborns completed the study.

For each newborn included in the study, detailed anamnestic data were collected, including gender, gestational age, birth weight and length, head circumference, Apgar score at the 1st and the 5th minute, data on multiple (twin) pregnancies, data on the mode of delivery, and cranial ultrasound findings. Cranial ultrasound findings were categorized as follows: US 1—normal finding; US 2—hyperechogenicity of the brain parenchyma lasting up to 14 days; US 3—hyperechogenicity of the brain parenchyma lasting more than 14 days; US 4—intraventricular hemorrhage; US 5—periventricular leukomalacia.

Assessment of spontaneous motor activity was performed according to the basic principles of Prechtl's method. The assessment of spontaneous motor activity was conducted by a trained individual with a valid license for evaluating spontaneous motor activity, based on video analysis.

A video camera was used to record the video. Necessary conditions for an adequate video recording included the relaxed awake state of the newborn: absence of crying, open eyes, irregular respiration, and the presence of movements. Given that behavioural states are not established before the 36th week of postmenstrual age, preterm infants below 36 gestational weeks were recorded during movement episodes, regardless of whether the newborn was awake or asleep. During the recording, the newborns were in a supine position on a flat surface (bed, mat), in diapers or minimal clothing to ensure unrestricted movement, with the face constantly visible and without a pacifier. During video recording, all distracting items from the environment, such as noise, the presence of parents and other people, toys, colourful blankets, mirrors, and similar objects, were removed. The room temperature was appropriate for the newborn's age and clothing.

For the assessment of spontaneous motor activity in the fidgety period, newborns were recorded between 50 and 54 weeks PMA. For this period, three types of movements were defined:

- F—Fidgety movements, movements of small amplitude, moderate speed, and variable acceleration, occurring in the head, neck, trunk, as well as the extremities, primarily in the distal parts (radio-carpal and talo-crural joints). They manifest continuously in the awake infant, except during crying. They can be observed as early as the 6th week post-term, but usually appear around the 9th

week and are present until the 20th week or even a few weeks longer.

● F—Absence of fidgety movements represents motor activity where the described fidgety movements are not registered.

● AbF—Abnormal fidgety movements look like normal fidgety movements, but their amplitude and speed are moderately or significantly greater.

The definitive neurological outcome was assessed based on a detailed neurological examination at 24 months of age (corrected calendar age). The examination was conducted by a well-trained and experienced neurologist specializing in paediatric neurology. The examination included a detailed assessment of muscle tone, reflexes, posture, and movements. The neurological outcome was classified as follows:

●Normal (completely normal neurological findings);

●MND—minimal neurological dysfunction, according to TINE criteria (Touwen Infant Neurological Examination) or nonspecific signs without clear and definitive signs of cerebral palsy;

●CP—cerebral palsy according to SCPE criteria (6, 7).

For subjects who exhibited motor deficits corresponding to CP at the age of 2 years, the neurological examination was repeated, and the definitive diagnosis was made at the age of four years according to the previously described SCPE criteria (6, 8).

Statistical data analysis was performed using SPSS 16.0 software. Mann–Whitney and Kruskal–Wallis tests were used to compare the values of continuous variables between groups. Proportions of categorical variables between groups were compared using the Pearson Hi2 test. To evaluate the diagnostic value of the assessment of spontaneous motor activity of newborns and infants in predicting the outcome after 24 months, the following were used: sensitivity, specificity, prevalence, positive predictive value, negative predictive value and 95% confidence interval (CI). Statistical significance was defined as p-value < 0.05.

Results

Table 1 presents the clinical characteristics of the participants, as well as their relation to the final neurological outcome at 24 months of the corrected calendar age. The final neurological outcome of the participants is categorized as normal, MND, and CP. Statistically significant outcomes associated with CP were observed more frequently in preterm infants born before 30 weeks of gestation, those with very low birth weight and length, and those with low Apgar scores at the 1st and 5th minute. Other monitored characteristics did not statistically significantly affect the neurological outcome at 24 months corrected calendar age.

The prevalence of general movements (GMs) in the observation period of 50–54 weeks of gestational age significantly differs concerning the neurological outcome after 24 months ($p < 0.001$). One hundred percent of participants who exhibited normal fidgety movements during this period had normal neuromotor development. In the CP group, there were no participants with normal presentation of fidgety movements. During the same observation period, among participants with a final neurological outcome of MND at 24 months, 73% showed abnormal fidgety movements (Table 2).

Table 1. Clinical characteristics of preterms in relation to neuromotor outcome after 24 months

Clinical characteristics	Outcome after 24 months				
	Normal	MND	CP	Summarized	p
Gestational age	35 (35–36) GW	35 (33–35) GW	29 (27–29) GW	35 (34–36) GW	< 0.05
< 30 weeks	2%	–	100%	10%	< 0.001
≥ 30 weeks	98%	100%	–	90%	
Gender					
Female	48%	45%	57%	49%	n.s.
Male	52%	55%	43%	51%	
Twins					
No	74%	82%	100%	77.5%	n.s.
Yes	26%	18%	–	22.5%	
Caesarean section					
No	65%	55%	43%	61%	n.s.
Yes	35%	45%	58%	39%	
Birth weight (g)	2150 (2000–2350)	1750 (1350–2400)	1320 (1250–1350)	2125 (1800–2350)	< 0.01
Birth body length (cm)	45 (42–47)	44 (43–45)	39 (35–40)	44 (42–47)	< 0.05
Head circumference (cm)	30 (29–32)	30 (28–32)	28 (26–29)	30 (28.5–31)	n.s.
Apgar score (1st minute)	8 (8–9)	8 (8–8)	6 (1–7)	8 (8–9)	< 0.001
Apgar score (5th minute)	9 (8–9)	8 (8–8)	7 (5–8)	9 (8–9)	< 0.001

n.s.—non significant

Table 2. General movements of preterms in the fidgety period in relation to neuromotor outcome after 24 months

	Outcome after 24 months				
GMs 50–54 gestational weeks	**Normal (n = 62)**	**MND (n = 11)**	**CP (n = 7)**	**Summarized (n = 80)**	**p**
F	62 (100%)	–	–	62 (72.5%)	< 0.001
AbF	–	8 (73%)	–	8 (10%)	
F-	–	3 (27%)	7 (100%)	10 (12.5%)	

To further determine the significance of normal findings, i.e., fidgety movements in the period of 50–54 weeks of gestational age, the diagnostic value of this finding in predicting CP as a final outcome was evaluated (Table 3). Without any test, the probability of developing CP was 8.8% (95% CI; 3.6–17.2%). If the GMs findings were normal during the 50–54 weeks of gestational age, the probability that the participant would have CP as a final outcome was 0% (95% CI; 0–5.8%). Without any test, the probability that the participant would not develop CP was 91.2% (82.8–96.4%). If the GMs findings were abnormal during the 50–54 weeks of gestational age, the probability of the participant not developing CP as a final outcome was 61.1% (35.8–82.6%).

Figure 1 shows that significant deviations from normal intracranial ultrasound findings were the least in the group of participants who had a normal final neurological outcome. The greatest deviations were observed in the group of participants with CP as the final neurological outcome ($p < 0.001$). Pathological or altered intracranial ultrasound findings statistically significantly differed between groups with final neurological outcomes (normal, MND, CP) ($p < 0.05$). Altered findings were most common in participants with CP and least common in those with a normal neurological outcome.

Table 3. Evaluation of the diagnostic value of normal findings during the observation period in predicting the development of CP in the final neurological outcome

Normal finding GMs 50–54 gestational weeks	**CP**		**Summarized**
	Yes	**No**	
Yes		62	62
No	7	11	27
Summarized	7	73	80
Sn	0% (95% CI; 0–41%)		
Sp	15.1% (95% CI; 7.8–25.4%)		
Prev	8.8% (95% CI; 3.6–17.2%)		
PPV	0% (95% CI; 0–5.8%)		
NPV	61.1% (95% CI; 35.8–82.6%)		

Sn—sensitivity; Sp—Specificity; Prev—prevalence; PPV—positive predictive value; NPV—negative predictive value

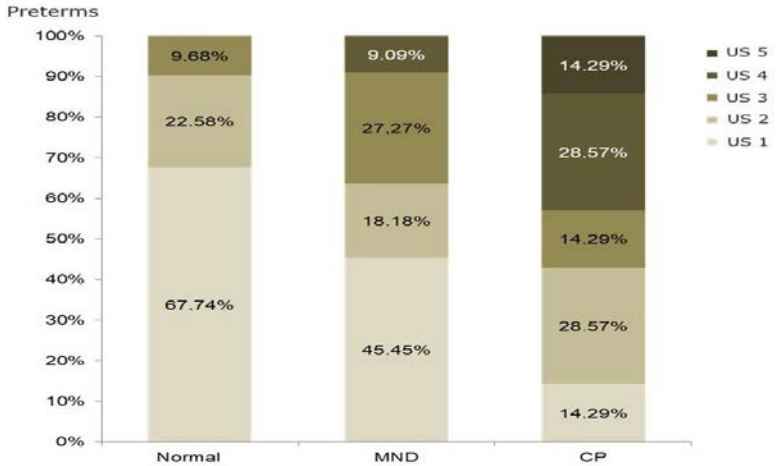

Figure 1. Neurological outcome of preterms in relation to intracranial ultrasound findings (by categories)

Discussion

In this study, the assessment of spontaneous motor activity was performed on newborns belonging to the preterm infant group. The reason for selecting this group is the fact that preterm infants have a higher chance of neuromotor developmental deviations, making their identification a significant challenge (9–14). According to this study, preterm infants with very low birth weight and length, those born before the 30th gestational week, and those with a low Apgar score at the 1st and 5th minute have a higher chance of these deviations. Similar results were published previously (15–17).

This study was performed during the period of fidgety movement manifestation, specifically at the time when the most intense presentation of these movements is expected, between 50–54 weeks postmenstrual age (PMA). The final neurological outcome was assessed at the age of 2 years (corrected calendar age—CCA). For subjects who exhibited motor deficits corresponding to CP at the age of 2 years CCA, a repeated neurological examination was performed, and the definitive diagnosis was established at the age of four years according to the SCPE criteria (8).

The earlier manifestation of fidgety GMs is characteristic of preterm infants. Numerous experiments have been conducted to investigate the effects of visual, acoustic, social, and proprioceptive stimuli on the quality and timing of fidgety movements. No stimulus changes the quality of fidgety movements. Prechtl et al. studied the fidgety movements of completely blind infants with no evidence of brain injury. The research showed an increased frequency of fidgety movements, and Prechtl et al. concluded that this was a form of compensation due to the lack of visual integration. Prechtl considered that fidgety movements represent a precise adjustment of the proprioceptive system (18).

We can wonder if newborns and infants with normal presentation of spontaneous movements can have a pathological neurodevelopmental outcome. Recent studies have shown that such cases are rare but do exist (19, 20). The pathological outcomes range from mild forms of CP to ADHD syndrome, particularly in high-risk infants who have shown normal fidgety movements. In the present study, this was not the case. The evaluation of diagnostic value in this study concluded that if the finding was normal, i.e., if there was a presentation of F GMs, the probability of CP as the final neurological outcome was 0%. This data confirms the high predictive value of F GMs, which is also supported by eminent experts in the field of GMs (21).

Fidgety movements also have their pathological forms. One of them is AbF GMs. In this study, AbF GMs were registered in 8 preterm infants. The results of this study indicate that AbF GMs have low predictive value for the development of CP. They also indicate that the probability of an infant with AbF GMs developing CP as the final outcome is 0%. All subjects in this study who had AbF GMs developed MND as the final neurological outcome. Similar studies have been conducted by other researchers. Einspieler et al. investigated AbF GMs as an early marker for MND (22). They concluded that AbF GMs have low predictive value for the development of CP and complex forms of MND. This movement manifestation has good predictive value for the simple form of MND, which involves a lack of fine motor skills.

In this study, all 10 subjects who had registered F- GMs during the observation period had a neurological deficit as the final neurological outcome, with 7 subjects having CP and 3 subjects having MND. This result is consistent with previous research (23–25). All previous studies that have examined GMs have confirmed the high predictive value of F- GMs. They have shown that infants who do not exhibit F GMs during the expected manifestation period have a high risk of developing neurological deficits later in life. Morgan et al., in their study conducted in Australia on 259 subjects, registered F- GMs in 48 of them. Of these 48 subjects, 39 developed CP as the final neurological outcome, while the remaining 9 also did not have a normal neurological outcome, instead showing neurological deficits of the MND type (26). Burger et al. systematically analyzed 17 studies on the predictive value of fidgety movements, particularly the absence of fidgety movements. A total of 1926 subjects were observed, of which 90% belonged to the preterm group. The subjects were followed up to the age of 12–24 months corrected calendar age. The conclusion of their study is the high sensitivity and specificity for fidgety movements (sensitivity 98%, specificity 94%) (27). In a similar study on the predictive value of fidgety movements, Romeo et al. published identical results in their study on 900 newborns (28).

Comparing the ultrasound (US) findings of the brain with the final neurological outcome in this study, it can be concluded that a normal US finding does not have a high predictive value for later neurological deficits and the development of MND and CP. The results of this study indicate that subjects with normal US brain findings can have a pathological neurological outcome, which correlates with previously described studies. Additionally, the results of this study suggest that a pathological US finding has predictive value for later neurological deviations. A pathological US finding is statistically significantly more frequent in subjects who had CP as the final outcome ($p < 0.05$). All obtained results are consistent with Prechtl's studies on the predictive value of US brain findings. Prechtl concluded that the finding of increased echogenicity of brain tissue has a transient character and weak prognostic value, especially if it lasts less than two weeks. It is important to emphasize that despite the utility and necessity of US diagnostics, studies have described cases of children diagnosed with CP who had normal US brain findings in the first months of

life (29). Certainly, an abnormal US finding in most cases necessitates an MRI examination and further monitoring (13, 30).

Conclusion

The results of this study confirm the practical importance of assessing general movements and the need for developmental follow-up for all preterm infants. A finding indicating normal general movements during the 50–54 weeks of age, resulted in a normal outcome for all subjects after 24 months. Such a high predictive value of this finding suggests the need for wider application of this method and, consequently, the need for the education of professionals.

Early detection of any neurological deficit symptoms is crucial as it allows for the timely inclusion of children in neurodevelopmental treatment, contributing to the improvement of functional motor status at a later age, considering the biological phenomenon of brain plasticity.

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PROCENA SPONTANE MOTORIČKE AKTIVNOSTI U PREDIKCIJI NORMALNOG NEUROMOTORIČKOG RAZVOJA KOD PREMATURUSA

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Konvencionalne metode neurološke procene novorođenčadi i odojčadi upotrebljavaju se u svakodnevnoj kliničkoj praksi. Budući da kod prevremeno rođene dece postoji više faktora rizika za nastanak neuromotoričkih razvojnih poremećaja, cilj ovog istraživanja bio je da se utvrdi prediktivna vrednost spontane motoričke aktivnosti za normalan neurološki i funkcionalni ishod u uzrastu od 24 meseca kod prevremeno rođene dece u tzv. *fidgety* periodu.

Studija je sprovedena kao prospektivna klinička studija i obuhvatila je osamdesetoro prevremeno rođene dece. Procena spontane motoričke aktivnosti vršena je prema osnovnim principima Prechtlove metode u periodu od 50. do 54. nedelje postmenstrualnog uzrasta.

Svi ispitanici kod kojih su evidentirani normalni *fidgety* pokreti imali su i uredan neuromotorički nalaz u uzrastu od 24 meseca. Među decom koja su kao konačan neurološki ishod imala nalaz minimalne neurološke disfunkcije nakon 24 meseca, 73% njih pokazalo je abnormalne *fidgety* pokrete. U istraživanju nije bilo ispitanika kod kojih je uočena normalna prezentacija *fidgety* pokreta, a kod kojih su u uzrastu od 24 meseca evidentirani neurološki deficit i klinička slika koja ide u prilog kasnijem razvoju cerebralne paralize. Veće šanse za razvoj neurorazvojne devijacije imaju deca rođena pre termina sa (veoma) malom porođajnom težinom, prematurusi rođeni pre 30. gestacijske nedelje, kao i deca sa niskim vrednostima Apgar skora.

Visoka prediktivna vrednost nalaza normalne spontane motoričke aktivnosti u periodu od 50. do 54. nedelje postmenstrualne starosti potvrđuje praktičnu važnost procene spontane motoričke aktivnosti i potrebu za praćenjem razvoja sve prevremeno rođene dece.

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***Ključne reči**: prevremeno rođena deca, spontana motorička aktivnost, Prechtlov metod, neurorazvojni ishod*