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Development of an Infant's Peripheral Motor System Within the First 3 Years of Life as Studied Using Surface Electromyography

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Relevance. Clinical assessment of condition of the neuromuscular system of a growing body is difficult in practice due to lability and instability of many neurological symptoms. **Objective.** Analysis of a child's peripheral neuromuscular system development from the 33rd gestational week to the end of 3 years (36 months) of postnatal life. **Methods.** The authors conducted a longitudinal sampling study observing the stratified randomization principles. The subjects were stratified by gestational and postnatal age, sex and neurological status. **Results.** The authors studied premature (31-32 gestational weeks) and term (38-39 gestational weeks) infants. Interference electromyograms (iEMG) of a premature infant within the first 6 weeks of life and a term infant within the first days of life were similar and characterized by "simplified" time structure, low amplitude and frequency. The dynamics of iEMG parameters in premature infants was low. Rapid increase in the non-linear iEMG parameters in term infants in the first year of life reflected on the complication of the iEMG signal. Linear iEMG parameters would monotonously increase in the course of the year. Maximum changes of the non-linear and linear analysis parameters were observed at the age of 6 month, which is a crucial period of development of corticospinal tracts and establishment of voluntary manipulative motions. **Conclusion.** The obtained data indicate importance of the first 2 weeks of life for the development of a term infant's musculoskeletal system, within which a "mature" type of the motor neuron pool organization is formed. At the same time, quantitative changes observable in the iEMG (amplitude increase) continued throughout the 36 months of the study and indicate a continuing growth of skeletal muscles. iEMG of premature infants are peculiar in that they show a simpler time organization, which indicates a continuing "intrauterine" pattern of the motor neuron pool functioning.

Keywords: premature infants, term infants, non-linear and linear parameters, electromyography, neuromuscular status.

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INTRODUCTION

Prolonged stage of postnatal development of human locomotor system, including development of skeletal muscles and nerve centers, has been described [1]. However, the aforementioned

development processes have a range of regularities not time-matched (asynchronous) with crisis periods of the body development in general [2]. Neuroevolutionary concept of nervous system development explains these regularities primarily with ontogenetic adaptation, which represents a change of physical activity for adequate body adaptation to internal and external condition on different stages of ontogenesis [3]. Functional consistency of physical activity in a fetus, a neonate and an infant is an appropriate example; it should be noted that the dramatic process of delivery is not a significant factor neither of formation of specific types of physical activity, reactions and reflexes and nor of decrement of other types of physical activity, reactions and reflexes [4, 5].

Morphological development of human locomotor system has been described in various sources widely and in detail [6, 7]. Both physiological and morphological properties of motor units are susceptible to alteration after birth [8-11]. Peculiarities of nervous system morphology in fetuses and neonates are non-simultaneous development of its structures, immature neuronal apparatus and interneuronal contacts, low velocity of signaling transduction via unmyelinated fibers and low discharge frequency [8]. Although most results were obtained by means of animal studies [8], there have been studies of infants recently. These studies show that interference electromyograms (iEMG) in 1-day-old children differ from adult iEMG considerably. In particular, such non-linear parameters as fractal and correlation dimension were considerably lower (1.35 and 4.0) than in adults (1.75 and 4.5, respectively) [4]. Moreover, these parameters considerably changed even within the first 4 days; this indicates sensitivity of these parameters to intrauterine factors [12]. It is also known that turn-amplitude parameters of infants change throughout the first year of life [13]. It is obvious that these data are not sufficient to understand ontogenesis of a growing body's motor system.

On the other hand, considerable attention is given not only to morphological peculiarities, but also to functional condition of a child's physical sphere (maximum muscular contraction velocity, force and rate, precision in movement), which may be evaluated when the child reaches the age of 3-6 years [14]. Movement function dynamics testing in infants involves such motility parameters as muscle tone, deep periosteal and tendon reflexes, labyrinthine and tonic neck reflexes, passive and spontaneous movements [2]. One of the most significant characteristics not only of the neonate's nervous system condition, but also of the overall condition, out of the aforementioned is muscle tone. It may change depending on the child's body type, gestational age, level of consciousness and physiological condition, that is why it is important not to ignore the risk of deviant or borderline lapses of the neurological state, especially in the first 3 months of life. As for labile periosteal reflexes in neonates, their assessment in isolation from other parameters yields little information [15]. Thus, diagnosis of a growing child's nervous system may be complicated, as different neurological phenomena may be seen as optimal or suboptimal in different conditions and at different age [2]. The theory of "classical" neurology, which defines each phenomenon categorically as "normal"/"abnormal", "pathological", becomes inefficient for neurology of a growing body [2].

Our study **was aimed at** analyzing development of the peripheral segment of a child's locomotor system starting from gestational week 33 up to 3 years (36 months) of postnatal life on the basis of the current data.

STUDY METHODS

Study design

Longitudinal sampling study observing principles of stratified randomization. Stratification concerned gestational and postnatal age, sex and neurological state.

Inclusion criteria

Inclusion criteria for a neonate group: gestational age (GA) – 31-32 weeks; postnatal age – 2, 4, 6 weeks; low risk – absence of severe deviations of the child's somatic and neurological state [2].

Inclusion criteria for an infant group: GA – 38-39 weeks, postnatal age – 0-1, 1-3, 3-6, 6-9, 9-12, 12-24 and 24-36 months; health group II.

Exclusion criteria for study groups: severe condition, respiratory disorders, moderate or severe hyperbilirubinemia, generalized infection, congenital heart defects, moderate or severe anemia, fetal growth restriction, moderate or severe perinatal CNS lesion, active rickets, protein-energy malnutrition (hypotrophy), obesity, skin and hypoderm diseases.

Study description

The study involved analysis of ante- and intranatal anamnesis, anthropometric data, type of feeding, accompanying pathologies, neurological state and use of electromyographic methods. Skin non-invasive electromyography (EMG) with new non-linear and traditional linear signal parameters was used to for this purpose [4, 16, 17].

Study site

Children were examined at State Budgetary Healthcare Institution (SBHI) “Republican pediatric hospital” (Petrozavodsk) after obtaining informed consent of their mothers and approval of the Ethics Committee of the Ministry of Health of the Republic of Karelia.

Registration methods

In order to register electromyograms, pickup superficial bipolar electrodes (LLC “Neurosoft”, Ivanovo, Russia) would fix with a researcher's hand or rubber band along the muscle fibers. Ground electrode would be located around the child's wrist joint or the lower third of the shin or pressed against the skin with a hand without the doctor touching the child's skin. Electrolyte-containing gel would be put between the skin and the electrodes for better conduction of electric signals. Electromyographs Neuro-MVP-4 and Neuro-MVP-Micro (LLC “Neurosoft”, Ivanovo, Russia) were used to amplify EMG-signals. Analog-to-digital converter's sampling frequency was 20 kHz, frequency bandwidth – 50-1,000 Hz. Electromyograms would be recorded to a hard drive for subsequent processing successively (four large muscles of an upper limb and a lower limb [right arm and left leg] with subcutaneous localization): *m. biceps brachii* and *m. triceps brachii*; *m. tibialis anterior* and *m. gastrocnemius*.

Data analysis

Non-linear iEMG analysis was conducted by means of FRACTAN 4.4 (Institute for National Security of the Russian Academy of Sciences, Pushchino) and concerned the following parameters:

- 1) fractal dimension (D);
- 2) correlation dimension (D_c);
- 3) correlation entropy (K_2).

Fractal dimension is measure of the space-filling capacity of the electromyographic curve plane and allows evaluating internal interrelations of the non-linear process and the measure of iEMG self-similarity [18]. Complexity of a dynamic system's behavior and the number of system-controlling factors are characterized by correlation dimension (D_c). The higher the D_c , the more complex the signal and the more parameters (equations or signal generators) control it. Correlation entropy (K_2) reflects the degree of loss of information about the system with time. In

practice, K_2 operates as information dimension and quantitatively characterizes the degree of system chaotization and indicates how quickly the system becomes hardly predictive. High K_2 shows that the signal is unpredictable. In general, all three non-linear parameters demonstrate orderliness of the signal and, in the end, degree of synchronization of motor neuron (motor units) activity.

Linear iEMG analysis was used to analyze the mean maximum amplitude (A, mcV) and mean frequency (MNF, Hz).

Study conditions

Children were analyzed when conscious between feedings carefully observing thermal conditions, since low ambient temperature may cause muscle hypertonia and tremor, high ambient temperature – muscle hypotonia. iEMG recording in 0-2-week-old premature infants was conducted at the ward in a couveuse (air temperature – 32 °C, humidity – 40%). Body temperature was controlled by means of a skin servocontroller. 4-6-week-old children were examined on a swaddling table (box air temperature – 24-25 °C, low constant air speed – 0.1 m/s). Term infants and under-3 children were examined at a neurophysiology office on a banquette after 1-2-minute adaptation of an unswathed child to air temperature of 24-25 °C and constant air speed of 0.1 m/s. Peripheral body temperature was controlled by means of a digital thermometer (UT-102, A&D Company, Ltd., Japan) with 0.1 °C accuracy of measurements.

An algorithm of neurological examination of premature infants was tested to assess neurological state of premature infants [2]. Term infants were examined by means of a conventional pediatric algorithm [19].

Statistical analysis

Statistical data manipulation was conducted by means of Excel 2003, SPSS 12.0™ and Statgraphics Centurion 15.0. Kruskal-Wallis (W-test) and Mann-Whitney (U-test) tests were used to determine intergroup differences (between age groups and different groups of children).

RESULTS

Study participants

The study involved 3 groups of neonates. Each group had an equal number of girls and boys:

- 1) premature infants with low risk; GA – 31-32 weeks; postnatal age – 2, 4, 6 weeks (33, 35, 37 weeks of postconceptional age [PCA]); 30 examinations, 120 EMG sessions;
- 2) term infants without neurological deviations; GA – 38-39 weeks; postnatal age – 2, 4, 6 weeks; 30 examinations, 120 EMG sessions;
- 3) term infants without neurological deviations; age – 1,5-36 months (3 years); 120 examinations, 480 EMG sessions.

Infants were examined with due regard to the term of antigravity system maturation [1] at the age of 1.5-3 (20 examinations, 80 EMG sessions), 3-6 (20 examinations, 80 EMG sessions), 6-9 (20 examinations, 80 EMG sessions), 9-12 (20 examinations, 80 EMG sessions), 12-24 (20 examinations, 80 EMG sessions) and 24-36 (20 examinations, 80 EMG sessions) months.

Peculiarities of study groups

Accompanying pathologies were the same in groups of premature and term infants: mild conjugation jaundice, atopic dermatitis, urinary tract infections, mild iron-deficiency anemia and

hydrocele. Urinary system infections, mild anemia and small-scale cardiac anomalies prevailed in children aged 2-3 years.

Clinical evaluation of 0-6-week-old premature infants on the basis of a neurological examination algorithm revealed the following peculiarities. The optimal development value (≥ 32 points) at 2 weeks of age (33 PCA weeks) was observed in 20% of the children, normal development value (≥ 26.5 points) – in 80%. Some neonates had asymmetric muscle tone: 10% - in upper limbs, 30% - in lower limbs. The maximum development value was observed at the age of 4 weeks (35 PCA weeks) – in 30% of the children. Asymmetric leg muscle tone was diagnosed in 10% of the examined children. The maximum neurological development value at 6 weeks of age (37 PCA weeks) was observed in 50% of the children, optimal development value – in 40%, normal development value – in 10%.

The following clinical peculiarities of the locomotor system were revealed in infants. Spontaneous physical activity alterations were observed in 25% of the cases: reduction – 12%, increase – 10%, asymmetric movements – 3% of the children. Muscle hypotonia was observed in 5% of the children, hypertonia – in 12%, asymmetry – in 6%; 94% of the children featured unaltered periosteal reflexes. Evaluation of reflexes of the neonates from the corresponding age groups revealed intensification or inhibition thereof in 12% and 5% of the cases, respectively. Muscle hypotonia was detected in 10% of the 12-24-month-old children, asymmetric muscle tone – in 20%. 5% of three-year-old children had moderate muscle hypotonia. The obtained results indicate deviant neurological state of infants, not always serve as a pathophysiological phenomenon and correlate with impact of various brain structures on the peripheral segment of the growing body's locomotor system.

Non-linear iEMG parameters

iEMG fractal dimension (D) in premature infants of 33 PCA weeks (2 postnatal weeks) was the same in all the analyzed muscles – 1.5-1.64 (standard deviation – one sigma). Correlation dimension (D_c) and correlation entropy (K_2) were 4.0-5.0 in all the analyzed muscles (pics. 1, 2). These values are significantly lower than similar parameters in term age-peers: D – 1.74-1.85, D_c and K_2 – 6.4-9.9. Thus, non-linear parameters grow for 4 weeks in premature infants (see pics. 1, 2).

In contrast to premature infants, iEMG parameters in term infants become high by week 2 of postnatal life and change little in the subsequent 4 weeks. At the same time, it is known that all non-linear parameters are very low in 0-1-year-old term infants (D – 1.35-1.45, D_c and $K_2 \sim 2.5$ -4.0) [4] (see pics. 1, 2). This means that the first two weeks of life are characterized by an abrupt surge of non-linear parameters, which do not change much until the adult age [20].

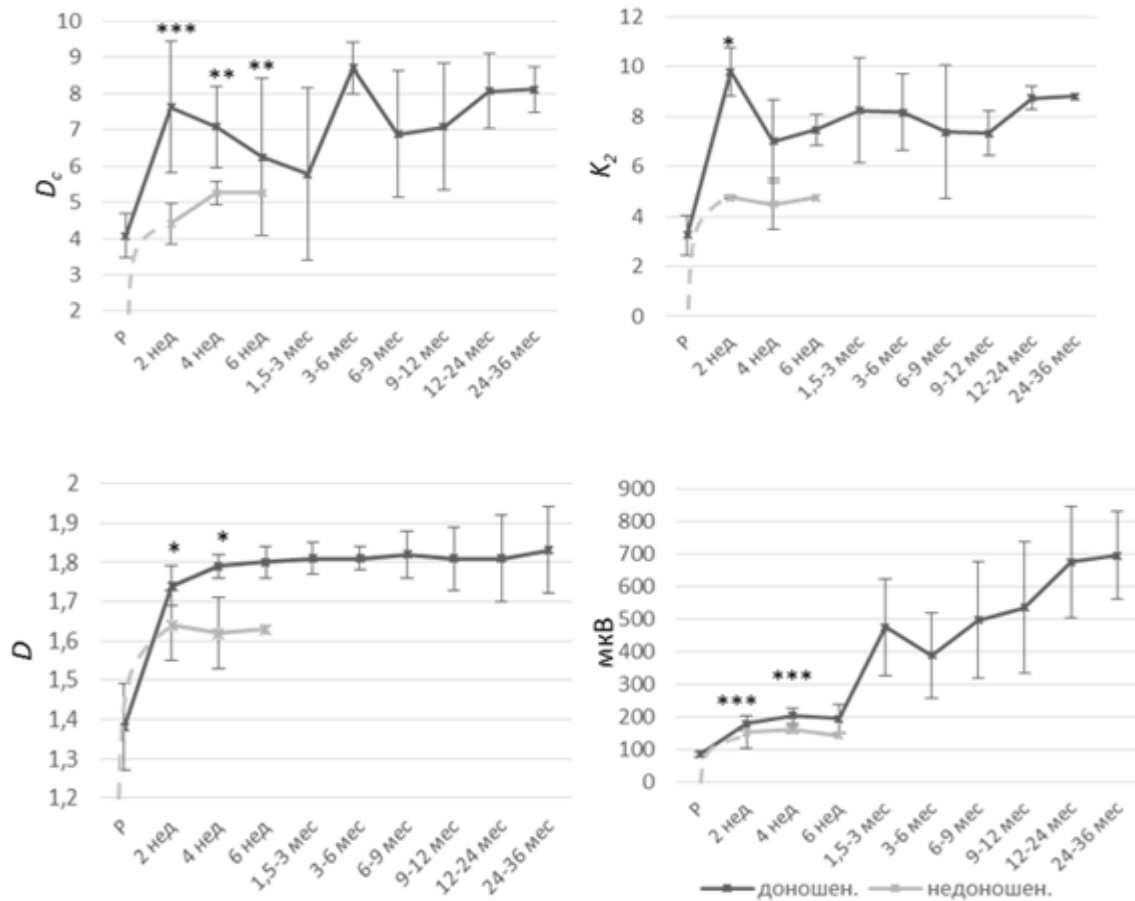
Non-linear parameters generally grow within the first year of life of term infants: D_c is at its peak at the age of 3-6 months (5.78-9.03), K_2 – at the age of 6-9 months (8.23-9.7). D remained virtually unchanged in the follow-up – 1.79-1.82. By the end of the 12th month of life non-linear parameters in healthy term infants were as follows: D_c – 5.36-7.77, D – 1.76-1.83, K_2 – 7.34-9.0. Subsequently, by the age of 24 and 36 months, only D_c changed insignificantly (6.91-7.99 and 6.84-8.4, respectively). Other non-linear parameters remained virtually unchanged (see pics. 1, 2).

Linear iEMG parameters

Maximum iEMG amplitude in premature infants at the age of 33 PCA weeks was 130-173 mcV (standard deviation – one sigma), average spectrum frequency – 166-185 Hz. In term infants these parameters were higher – 181-230 mcV and 184-238 mcV, respectively (see pics. 1, 2). Linear parameters in muscles of arms and legs did not differ. Maximum amplitude noticeably changed within the first 6 weeks of life of premature infants only in *m. triceps brachii* – 160-300

mcV. At the age of 1.5-36 months maximum amplitude continued to increase in all muscles (see pics. 1, 2); the average spectrum frequency remained virtually unchanged.

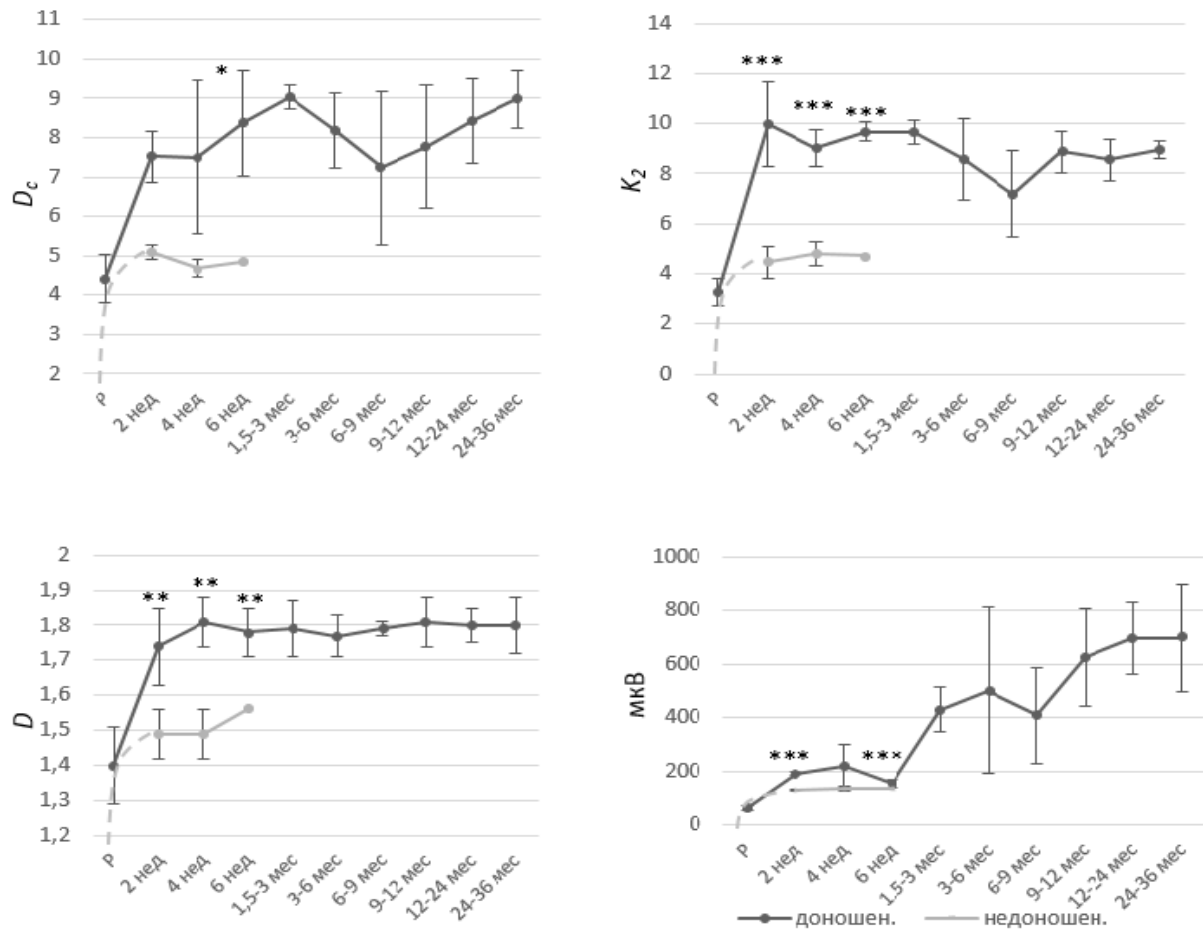
Pic. 1. Comparative dynamics of iEMG correlation dimension (D_c), correlation entropy (K_2), fractal dimension (D) and average amplitude (mcV) in *m. biceps brachii* in premature (aged 2-6 weeks) and term (aged 2 weeks – 36 months) infants.



Note. P – birth (0-4-day-old term infants). * - $p < 0.05$; ** - $p < 0.01$; *** - $p < 0.001$ (intergroup comparison of premature infants and their term age-peers).

нед Weeks
мес Months
мкВ mcV
доношен. Term infants
недоношен. Premature infants

Fig. 2. Comparative dynamics of iEMG correlation dimension (D_c), correlation entropy (K_2), fractal dimension (D) and average amplitude (mcV) in *m. gastrocnemius* in premature (aged 2-6 weeks) and term (aged 2 weeks – 36 months) infants.



Note. P – birth (0-4-day-old term infants). * - $p < 0.05$; ** - $p < 0.01$; *** - $p < 0.001$ (intergroup comparison of premature infants and their term age-peers).

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DISCUSSION

This article presents data on dynamics of interference electromyogram in 0-36-month-old term infants. We also obtained follow-up iEMG data in 2-6-week-old premature infants (33-37 PCA weeks). According to the common time scale, premature infants remained in “prenatal condition” and achieved the level of development observed in term infants immediately after birth only by the 6th week of age. Thus, this article attempts to look at the prenatal condition of the musculoskeletal system and analyze its development throughout the 3 subsequent years with the help of non-linear iEMG parameters. Non-linear parameters of various biosignals have been becoming widely used for analyzing physiological and pathological processes for the last decade [21-24], while the iEMG signal is considered adequate for understanding physiological processes occurring in a skeletal muscle [21].

The most significant finding of this article is that in term infants the time iEMG structure virtually reaches the adult-adequate parameters as early as in the 2nd postnatal week. This is demonstrated by high levels of all non-linear parameters (fractal and correlation dimensions, correlation entropy) in term infants from the 2nd postnatal week. E.g., fractal dimension in term infants in the framework of this study reached ca. 1.8 (in adults – 1.75 [20]) as early as in the 2nd postnatal week (see pics. 1, 2) and remained virtually unchanged for the following 36 months. Correlation dimension and entropy were characterized by similar dynamics (see pics. 1, 2). According to the literature, non-linear iEMG parameters in term neonates are significantly lower (see pics. 1, 2). E.g., fractal iEMG dimension in the first day of life is only 1.3-1.4 [12]. Non-linear parameters characterize temporal organization of the process, such as iEMG, from different perspectives. Low fractal dimension indicate a few iEMG events (kinks, self-similar structures, peaks), low correlation dimension – low complexity of the system (small number of controlling elements), low entropy – high predictability and orderliness of all processes, including the physiological process [24]. In general, these data indicate an abrupt surge in complexity of the generator (motor neuron pool), which creates the iEMG. Apparently, the operative factors capable of altering iEMG organization this heavily are gravity and lower temperature characteristic of intrauterine life [25, 26].

Neurophysiological interpretation of the obtained results is based on the data yielded by a study of activity of separate motor units (MU) and iEMG. In particular, it has been proven that iEMG entropy reduction is connected with increased synchronization of motor unit activity [27] and appearance of latent iEMG rates (also characteristic of MU synchronization) [17, 22]. It is interesting to note that such a classic linear iEMG parameter as amplitude monotonously grows throughout the first 36 postnatal months (unlike other non-linear parameters) (see pics. 1, 2). This indicates a continuous *quantitative* growth of musculoskeletal fibers in children in the setting of an already formed qualitative characteristic – iEMG complexity, i.e. organization of motor neuron pool activity.

The data on iEMG parameters of premature infants allow us to assume what happens inside the uterine when the fetus still remains in the amniotic fluid and is virtually exposed to immersion microgravity [26]. It has been established that non-linear iEMG parameters in premature infants are approximately twice as low as in their term age-peers. This indicates “simplicity” of the spinal iEMG generator, i.e. the motor neuron pool, in premature infants. It is known that high synchronization of MU activity causes higher muscle contraction force [28]; this may be an adaptive reaction in premature infants. After that, iEMG complexity slowly increases throughout 4 weeks (from week 2 to week 6), but does not reach the values typical for term age-peers. Methodological, administrative and ethical restrictions do not allow obtaining iEMG samples in 1-day-old premature infants. However, we may assume that non-linear iEMG parameters in such children are even lower (fractal dimension – ca. 1.0-1.1). Birth and, therefore, actualization of new intrauterine factors may lead to iEMG complexity growth in the first two weeks of life similar to the one observed in term infants.

CONCLUSION

Thus, the obtained data indicate importance of the first two weeks of life for development of musculoskeletal system of term infants characterized by formation of the “adult” type of the motor neuron pool organization. At the same time, quantitative iEMG changes (amplitude growth) continue throughout all the 36 examination months; this indicates a continuing growth of skeletal muscles. iEMG of premature infants is characterized by simpler temporal organization, which indicates a maintained “intrauterine” pattern of the motor neuron pool operation.

CONFLICT OF INTEREST

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