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EFFECTIVENESS EVALUATION OF TRANSLINGUAL NEUROSTIMULATION IN MOTOR REHABILITATION IN CHILDREN WITH SPASTIC DIPLEGIA

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Introduction. Cerebral palsy is one of the most common non-progressive neurological disorders caused by fetal or infant brain injury. Current rehabilitation for children with cerebral palsy involves a series of measures, including physical training, special massage techniques, physiotherapy, treatment by certain positions and postures, use of supporting orthoses and fixation devices for walking, and special orthopedic suits facilitating verticalization and motor activity of a child. Over the last few decades, computerized stimulators and robotics with virtual reality systems have been actively used in neurorehabilitation. However, most of these systems did not show significant efficiency in rehabilitation of children with cerebral palsy. In the last few years, different non-invasive electrostimulation techniques have been considered innovative and can be applied independently or in combination with existing procedures. One of such techniques is translingual neurostimulation.
Aim. This study aimed to evaluate the effectiveness of a combination of translingual neurostimulation and physical rehabilitation for children with cerebral palsy.
Materials and methods. In this study, we observed 134 children (63 girls and 71 boys) with spastic diplegia aged 2–17 years (mean age is 7.8 years old ± 0.3). Depending on the type of rehabilitation therapy, the patients were divided into two groups: active (main) and control. Active group consisted of 94 children who received standard restorative treatment in combination with translingual neurostimulation, whereas the control group consisted of 40 children who received only standard rehabilitation treatment without translingual neurostimulation.
Results. Both groups of patients showed positive dynamics; however, patients in the active group showed greater improvements as evidenced by all grading scales. Improvements were observed in children of all ages, and the results were mostly stable for 12 months.
Conclusion. Translingual neurostimulation is a novel approach to neurorehabilitation that shows promising results, in addition to its proven effectiveness and safety. As a result of neurostimulation, the patient's brain becomes more susceptible to the applied therapeutic procedures aimed at restoring motor control and formation of new motor skills, thereby markedly increasing the effectiveness of neurorehabilitation. This study broadens the perspectives in the use and further development of translingual neurostimulation in rehabilitation of children with cerebral palsy.

Keywords: cerebral palsy; neuroplasticity; motor functions; rehabilitation; translingual neurostimulation.

ОЦЕНКА ЭФФЕКТИВНОСТИ ТРАНСЛИНГВАЛЬНОЙ НЕЙРОСТИМУЛЯЦИИ В ДВИГАТЕЛЬНОЙ РЕАБИЛИТАЦИИ У ДЕТЕЙ СО СПАСТИЧЕСКОЙ ДИПЛЕГИЕЙ

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Введение. Детский церебральный паралич, несомненно, является одним из самых распространенных непрогрессирующих заболеваний нервной системы, в основе патогенеза которого лежит повреждение головного мозга плода или новорожденного. Реабилитация детей с церебральным параличом предусматривает комплекс мероприятий, включающих лечебную физкультуру, специальные методики массажа, физиотерапевтические процедуры, лечение определенными положениями и укладками, применение поддерживающих ортезов и фиксирующих аппаратов для ходьбы, специальных костюмов, облегчающих вертикализацию и двигательную активность ребенка. В последние десятилетия стали популярными компьютеризированные тренажеры и роботизированные комплексы с использованием виртуальной реальности. Однако на сегодняшний день лечение детей с церебральным параличом по-прежнему недостаточно эффективно. В последние годы появились различные методы неинвазивной электростимуляции, которую применяют независимо или в сочетании с традиционными процедурами. Одним из таких методов является метод транслингвальной нейростимуляции.
Цель исследования — оценить эффективность применения транслингвальной нейростимуляции в комбинации с методами физической реабилитации детей с церебральным параличом.
Материалы и методы. В исследовании приняли участие 134 ребенка со спастической диплегией в возрасте от 2 до 17 лет (средний возраст — 7,8 ± 0,3 года), из них 63 девочки и 71 мальчик. В зависимости от варианта восстановительной терапии пациенты были разделены на две группы — основную и контрольную. Основную группу составили 94 ребенка, которые получали стандартное восстановительное лечение в сочетании с транслингвальной нейростимуляцией; контрольную группу — 40 детей, которые получали только стандартное восстановительное лечение без транслингвальной нейростимуляции.
Результаты. У пациентов обеих групп наблюдалась положительная динамика, однако в основной группе улучшение было намного более выраженно по всем оценочным шкалам. Улучшение было зафиксировано у детей всех возрастов, достигнутые показатели практически не снижались в течение 12 месяцев.
Заключение. Транслингвальная нейростимуляция является новым и перспективным направлением в нейрореабилитации. Данный метод доказал свою эффективность и безопасность. В результате стимуляции мозг пациента становится более восприимчив к терапевтическим процедурам, направленным на восстановление моторного контроля и формирование новых моторных навыков, что существенно повышает эффективность нейрореабилитации. Настоящее исследование открывает широкие перспективы применения данного метода у детей с церебральным параличом.

Ключевые слова: детский церебральный паралич; нейропластичность; моторные функции; реабилитация; транслингвальная нейростимуляция.

Introduction

Cerebral palsy (CP) is one of the most common non-progressive diseases of the nervous system, the pathogenesis of which is attributed to the trauma occurring to the brain of a fetus or neonate. The main manifestations of CP include changes in muscle tone and impaired locomotor function, management of body balance, and motor coordination, which lead to persistent motor stereotypies and delay in motor skill development [1–3]. Rehabilitation of children with CP is one of the biggest challenges in neurorehabilitation. It has been proven that neuroplasticity is the basis of regeneration and compensation of functions in patients with CP and those with several other acute and chronic diseases of the nervous system. Neuroplasticity is the ability of a nervous tissue to change its structural and functional state under the influence of various endogenous and exogenous factors, despite a stimulus offset [4]. According to previous research, neuroplasticity is due to multifunctionality of neurons and a vertical hierarchy of convergence. The convergence of multiple impulses carrying different information to the same nerve cells advocates the multifunctional nature of neurons and other brain elements; this enables the restoration of impaired functions of the nervous system [4–7]. Neurorehabilitation includes a combination of both medical and socio-pedagogical activities aimed at not just reducing muscle spasticity and increasing movement amplitude but also restoring impaired functions and teaching a child with established motor stereotypies new daily life motor skills. Rehabilitation of children with CP involves physical therapy; special massage techniques; physiotherapy; fixation of limbs in certain positions using splints and other devices; use of supporting orthoses and other fixation devices for walking; and special suits, such as Adele, Atlas, and Gravistat, facilitating verticalization and physical activity of children with CP. In the past decades, many new methods of physical rehabilitation have been developed. These include various computerized simulators and robotic complexes using virtual reality technologies, [7] such as Lokomat, Motomed, and Armeo [8, 9]. Despite these technological advances, the current treatment modalities for children with CP are still largely inadequate. In some patients, a reduction either in muscle tone or synergy of antagonistic muscles may lead to a marked improvement in the quality of motor skills. However, these effects are reversible and do not lead to significant development of new motor skills, decrease in spasticity, or improvement in quality of life [10]. Methods such as noninvasive electrostimulation, which are used independently or in combination with traditional procedures [11–18], have opened new prospects in the treatment of CP. One such method is translingual neurostimulation (TLNS). It was developed in the late 1970s by Paul Bach-y-Rita, who was a professor of rehabilitation medicine and one of the founders of the modern concept of neuroplasticity, in his US-based laboratory. It was under his leadership that a device for the electrotactile stimulation of the tongue was created. This device significantly improved the ability of the human brain to restore its lost functions [19].

The purpose of this study is to evaluate the effectiveness of TLNS in combination with the existing methods of physical rehabilitation in children with CP.

Materials and methods

The study involved 134 children with spastic diplegia CP aged 2–17 years (mean age, 7.8 ± 0.3 years), including 63 girls and 71 boys. All patients and their representatives gave voluntary informed consents before participating in the study. The intelligence of the children was not affected, and they were able to follow all the instructions. Based on the type of rehabilitation therapy, the patients were divided into study and control groups. The study group consisted of 94 children who received standard restorative treatment in combination with TLNS, whereas the control group consisted of 40 children who received only the standard rehabilitation treatment without TLNS. Standard rehabilitation treatment included massage, simulation training, hydrotherapy, robotic mechanotherapy, and special therapeutic gymnastics — 10 daily classes lasting 20 min. TLNS was performed using a portable neurostimulator (PoNS) and included 10 procedures lasting 20 min twice a day, with an interval of 3 h.

Some patients in both the groups expressed a desire to repeat the therapy course with an interval ranging from 6 months to 1 year; 37 patients from the study group and 11 patients from the control group underwent a repeated therapy course. From the study group, 8 patients completed 3 courses and 2 patients completed 4 courses.

Translingual neurostimulation

PoNS is a new-generation device for inducing peripheral neurostimulation (Fig. 1), the effect of which is based on the impact on the most densely innervated tactile region, the tongue. The tongue is best suited for electrical stimulation because of the following favorable conditions in the oral cavity: constant pH, constant temperature, high electrical conductivity, high humidity, and low excitability thresholds compared to other areas of the skin.

Electrostimulation of the tongue is currently one of the most effective and safe methods of stimulating the central nervous system. The tongue area is characterized by the maximum density of mechanoreceptors per unit area and the minimum two-point discrimination thresholds of 0.5–1 mm for mechanical stimulation and 0.25–0.5 mm for electrical stimulation [4, 5, 7]. The two main cranial nerves (trigeminal and facial) transmit nerve impulses from the anterior surface of the tongue directly to the brainstem, thereby activating the trigeminal nerve nuclei (mesencephalic, sensory, and spinal) and simultaneously stimulating the adjacent nucleus of the solitary tract through the facial nerve. The cochlear nuclei, medulla oblongata, and cervical region of the spinal cord (C_1–C_3) are also directly affected. The secondary activation includes the reticular formation of the brainstem, locus coeruleus, vestibular nuclear complex, and ventral por-

Fig. 1. PoNS device

tion of the cerebellum. Several systems of global neurochemical regulation of brain activity, including the noradrenergic, dopaminergic, serotonergic, and acetylcholinergic systems, can also be activated by electrostimulation as their cores are located in the brainstem. Intensive and regular stimulation of existing neurons activates synaptic contacts, axons, and the whole complex of pre- and postsynaptic neurochemical mechanisms, which stimulates synaptogenesis, the formation of new contacts between neurons [4–7]. For neurostimulation, the tongue was placed on the PoNS electrode array. The patient then performed exercises designed to facilitate learning new motor skills, which consistently became more complex according to the patient's progress.

Therapeutic gymnastics

The course of therapeutic gymnastics consisted of three sets of exercises that were selected individually based on the clinical symptoms, mental development, and motor development of the patient.

The first set of exercises aimed at developing the patient's ability to sit independently and maintain their balance.

The second set of exercises aimed at developing the skill to maintain a vertical body position in space and control the position during acceleration or deceleration of the rectilinear movement, as well as during rotations and deviations.

The third set of exercises aimed at developing the skill of walking with and without support.

The effectiveness of the therapy was assessed before and after the treatment based on the following standard scales.

1. The Ashworth scale was used to assess muscle spasticity. The spasticity level was expressed on a scale of 1 (low) to 5 (very high). The spasticity of the upper (ASHH) and lower (ASHL) limbs was measured separately.
2. The functional motor scale (FMS) was used to assess the development of motor skills, the level of which varies from 6 (slight failure) to 1 (very strong deficit). The assessment was performed on patients who were able to behave freely and move short distances up to 5 m (for example, in a room, FMS 5), at a distance of upto 50 m (for example, at school, FMS 50), and at a distance of upto 500 m (outdoors, FMS 500).
3. To assess the safety, an electroencephalogram (EEG) was prepared. The presence or absence of epileptiform activity was assessed using functional tests over 20 min. The indication of epileptiform activity on the EEG was considered as a contraindication for participation in the study.

Statistical processing

The study used statistical tests such as the Wilcoxon matched-pairs signed-rank test for nonparametric analysis to compare paired values before and after the course of therapy for the same patients and the Mann–Whitney *U* test for comparing unpaired samples in the study and control groups. Statistical analysis was performed using the statistical software package (JMP 13, Statistical Discovery, SAS).

Results

The tests used in this study made it possible to evaluate the effectiveness of TLNS to reduce muscle spasticity in the limbs and promote development of motor skills in comparison to standard therapeutic gymnastics. The changes in the muscle tone, as measured using the Ashworth scale, before and after repeated courses of treatment are shown in Figure 2.

The trend toward decreased spasticity entirely correlates with the improved mobility in both the groups. In this study, the emphasis was placed on rehabilitating the lower extremities and the body, which are necessary for maintaining posture and balance in statics (sitting and standing) and dynamics while developing walking skills. The training program did not include special exercises to reduce spasticity or increase mobility of the hands.

The initial values of the spasticity index for the hands (2.7–2.8) were slightly lower than those for the legs (3.1–3.3). However, the tests for the spasticity of the hands and legs showed almost similar results, with a small decrease in the spasticity of the legs.

The control group showed a statistically significant decrease in the spasticity index of the hands and legs after the first course of therapy and a slight decrease after the second course. Interestingly, the baseline values in the control group were the same for both the hands and legs, indicating that after a break between the courses, the spasticity index returned to the initial level.

On the contrary, the study group showed a steady tendency toward decrease in the spasticity index, both in the initial state before successive therapy courses and after the courses, which indicates the cumulative nature of the neurostimulation effect in terms of reducing the level of spasticity.

After each course of therapy, the level of spasticity decreased by 13%–17% for the hands and by 17%–23% for the legs. The total decrease in the spasticity index after three consecutive courses of therapy reached 40%–60% or more compared to the baseline values. Despite a significant decrease in the spasticity index in the control group by 3%–11% for hands and 12%–17% for legs, the results in the study group were significantly better; the spasticity index of the patients in this group did not return to the initial level in the intervals between the courses.

Figure 3 presents the results of motor skills assessment on the FMS scale after each of the three courses of rehabilitation treatment in the study and control groups.

The first course of traditional therapeutic gymnastics resulted in a significant improvement in FMS 5 (+30%) and FMS 50 (+17%) scales but not in FMS 500 scale. Repeating the traditional course did not result in a significant improvement.

As a result of the first course, the study group showed statistically significant improvement in the quality of motor skills on FMS 5 (+59%), FMS 50 (+51%), and FMS 500 (+31%) scales.

The second course was also effective and led to a significant improvement in motor skills on FMS 5 (+29%), FMS 50 (+30%), and FMS 500 (+31%) scales. After the third therapy course, the study

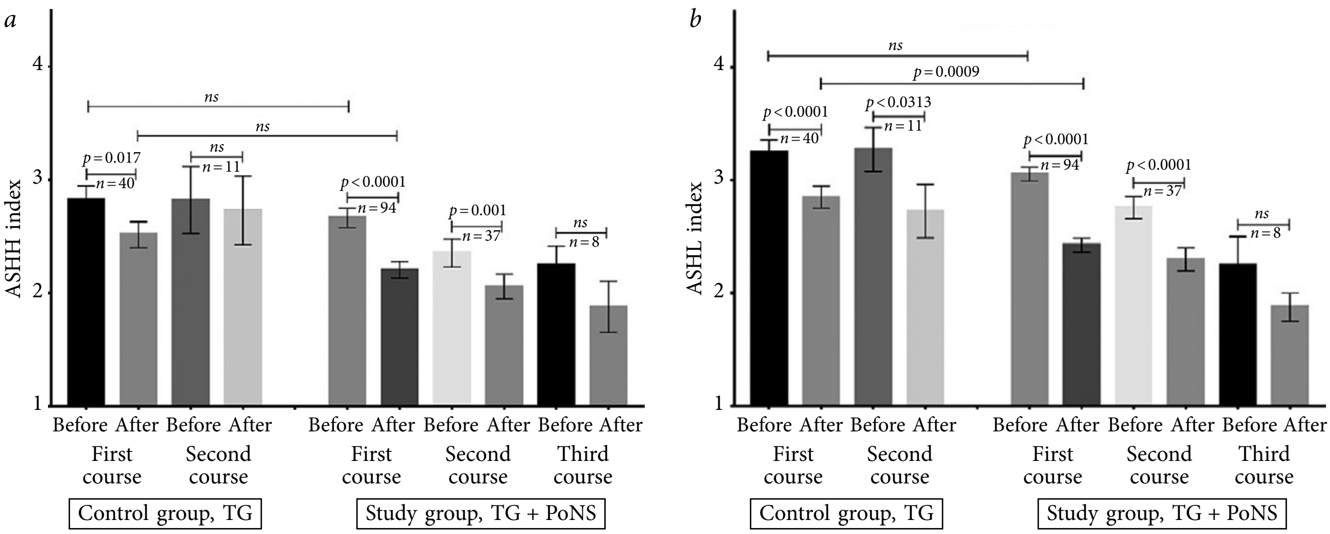

Fig. 2. The results of the Ashworth scale. *a* — spasticity of hands; *b* — spasticity of legs. TG — therapeutic gymnastics; PoNS — portable neurostimulator; *ns* — no statistically significant differences

Table 1

Numerical values of the results of the Ashworth scale

Group	Hand Spasticity Index, ASHH				Leg Spasticity Index, ASHL			
	Before	After	%	*p*	Before	After	%	*p*
Control group								
First course	2.8 ± 0.1	2.5 ± 0.1	–11	***	3.3 ± 0.1	2.9 ± 0.1	–12	***
Second course	2.8 ± 0.3	2.7 ± 0.3	–3	*ns*	3.3 ± 0.2	2.7 ± 0.2	–17	*ns*
Study group								
First course	2.7 ± 0.1	2.2 ± 0.1	–17	***	3.1 ± 0.1	2.4 ± 0.1	–23	***
Second course	2.4 ± 0.1	2.1 ± 0.1	–13	***	2.8 ± 0.1	2.3 ± 0.1	–18	***
Third course	2.3 ± 0.2	1.9 ± 0.2	–17	**	2.3 ± 0.3	1.9 ± 0.1	–17	*ns*

Note: ns — no statistically significant differences; ** $p < 0.01$; *** $p < 0.001$.

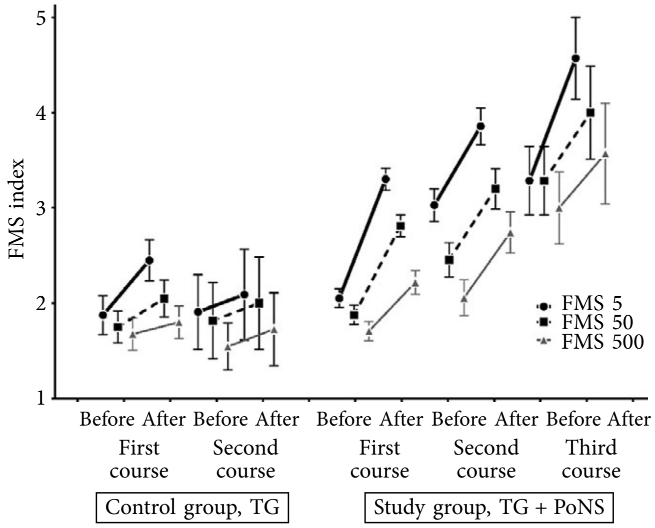

Fig. 3. The results of changes in motor activity according to the following scale of motor skills: FMS 5, 50, 500. TG — therapeutic gymnastics; PoNS — portable neurostimulator

group showed a continuous improvement in motor skills on FMS 5 (+40%), FMS 50 (+25%), and FMS 500 (+18%) scales. Despite the fact that the last two results were not statistically significant due to the small number of participants and the variability of the results, the overall positive trend in the improvement of motor skills when using neurostimulation was traced quite clearly (Fig. 3).

Discussion

TLNS is fundamentally different from other noninvasive methods of electrostimulation because it involves the activation of the brain mainly through the flow of nerve impulses generated naturally in the epithelium of the tongue and diverge throughout the central nervous system along natural pathways, as compared to other methods where unnatural external physical effects are exerted on certain areas of the cortex. The combination of TLNS and specialized exercises affects all components of motor activity, including the central (cortical), subcortical (basal ganglia, cerebellum, and brainstem), and spinal cord centers. With the help of multilevel neurostimulation, it is possible to control not only muscles but also complex sensorimotor functions, such as balance and coordination of movements while walking, which in combination with physical rehabilitation helps patients quickly master and develop new motor skills. The positive effects of TLNS persisted for up to a year between the therapy courses. This allowed us to consistently improve on the studied effects with every new course. In other words, neurostimulation gave rehabilitation a cumulative character. It is traditionally considered that a child with CP realizes half of his/her potential for developing motor skills by 5 years of age and a maximum of his/her potential by 7 years of age. In general, the results achieved at this age either remain stagnant or may worsen with age. In our study, a large number of children were older than 7 years; therefore, there are opportunities for expanding the application of this technology in the rehabilitation of children with CP and for improving the effectiveness of the therapy among older children.

This study showed that TLNS can enhance the effect of physical rehabilitation, most likely by means of activation of certain brain areas, improve the efficiency of existing neural networks, and stimulate synaptogenesis. No significant side effects were detected while using this stimulation; neither convulsive states nor convulsive readiness were recorded. The results obtained from the control group suggest that therapeutic gymnastics alone can lead to a statistically significant improvement in the condition of a child with CP to a certain extent (Fig. 2, 3). However, the observed improvements usually disappeared before the start of the second course of therapy. As observed in the tests, TLNS significantly improved the results of standard therapeutic gymnastics and increased the overall effectiveness of rehabilitation. After the first course, the study group showed a decrease in spasticity. Moreover, the motor skills of the children from the study group developed significantly better compared to those of the children from the control group. Improving motor skills is the main aim of neurorehabilitation. This method is aimed at developing new motor skills in patients and practicing them until they become involuntary, which in turn significantly improves their quality of life, level of socialization, and their overall capabilities. This method also provides new perspectives in planning for rehabilitation therapy as it produces a cumulative effect and allows for a consistent implementation of the rehabilitation plan. Positive and statistically significant changes obtained in all the tests distinguish this method from the other methods of neurostimulation, which mainly reduce spasticity but do not lead to the development of motor or walking skills or change the quality of life. In our study, we observed both a decrease in spasticity (according to the Ashworth scale, Fig. 2) and an improvement in motor skills (Fig. 3). Moreover, the magnitude of the changes after several consecutive courses of therapy indicates a possible change in the status (violations severity level) of a child with CP.

Conclusion

TLNS is an innovative, noninvasive method of neurostimulation of the central nervous system and a promising technique in the field of neurorehabilitation. This method has proven to be effective and safe. Children with spastic diplegia CP were treated with regular 20-min tongue stimulations in combination with modern physical rehabilitation methods for a period of 2 weeks. As a result of the treatment, the innate ability of their brain to develop motor skills was activated. Owing to the stimulation, the brain became more susceptible to therapeutic procedures aimed at restoring motor control and developing new motor skills; this markedly increased the effectiveness of neurorehabilitation.

We confirmed and evaluated the effectiveness of TLNS and its multidirectional impact on the central nervous system that allowed simultaneous improvement of physical, functional, and behavioral characteristics, such as motor coordination, balance, motor functions, and spasticity, in children with CP.

This study provides broad prospects for the development and application of this method in children with CP.

Additional information

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Conflict of interest. The authors declare that there is no obvious or potential conflicts of interest related to the publication of this article.

Ethical approval. This study was approved by the ethics committee of St. Petersburg State Municipal Hospital No. 40, protocol of the ethics committee No. 105 of December 7, 2017. All the patients (or their legal representatives) gave their consent to the participation in the study and the processing and publishing of their personal data.

Contribution of the authors

T.A. Ignatova and *G.A. Ikoeva* developed the concept and design of the study, analyzed the literature, collected and processed materials, and wrote the article.

Yu.P. Danilov and *A.P. Skoromets* developed the design of the study and edited the manuscript.

A.M. Sarana and *S.G. Shcherbak* edited the manuscript.

L.P. Kalinina and *V.G. Volkov* performed statistical analysis of the data.

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