

# Translingual Neurostimulation in Treatment of Children with Cerebral Palsy in the Late Residual Stage. Case Study

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**Keywords:** Translingual Neurostimulation, Portable Neurostimulator, Rehabilitation, Cerebral Palsy, fMRI, Neuroimaging.

**Abstract:** Management of cerebral palsy is an actual problem of modern medicine. A new direction of neurorehabilitation, intensively discussed in modern science and practice, includes various types of electrical stimulation. Constant stimulation of the nervous system is one of the most popular ways to activate neural networks in order to activate the brain and initiate neuroplasticity processes. Participants in the experiment were children with cerebral palsy, spastic diplegia form at the age of 6 to 19 (n=6) (mean age -  $17,9 \pm 5,6$  years). All subjects underwent standard treatment, including massage, therapeutic gymnastics simulators, robotic mechanotherapy, etc., which lasted 20-25 minutes with neurostimulation of the brain (using a PoNS device). All subjects underwent a functional brain imaging (MRI) before and after neurostimulation course. Results indicate positive dynamics in all subjects: most of them learned walking without aids, decreased muscle tonus and improvement in balance, coordination function were noted. Neurostimulation with the PonS device combined with curative gymnastics (focused exercises), improves the efficiency of motor functions and development of motor skills. Functional MRI with an active paradigm, with proper and high-quality performance, is an auxiliary method of objective control of treatment effectiveness.

## 1 INTRODUCTION

In subjects with cerebral palsy, there are obvious violations of equilibrium, position of motion, retention of the pose in space. Each function of the human body is based on well-organized complex neural networks, including numerous interconnected structures (cortex, nuclei, neural clusters) located in different levels of brain and spinal cord. Collaboration and synchronization of human performance in behavioral, cognitive and autonomic functions. This close integration is especially important in complex sensory and motor functions, such as vision, hearing, balance, gait, speech.

Neurorehabilitation of children with cerebral palsy is multicomponent and includes physiotherapy, special massage therapy, treatment, special limb treatment with different stitches, the use of fixing devices for walking, special, facilitating the motor activity of the child, and costumes. In modern medicine, the problems of rehabilitation of children

with cerebral palsy are given particular attention. A new direction of neurorehabilitation, intensively discussed in modern science and practice, is the use of various types of electrostimulation, as well as their use in or in combination with existing procedures. The most common among them - electrical stimulation of muscles and nerves, as well as the spinal cord. Electrical stimulation was used to treat spastic Erb-Duchenne paralysis in 1871. Since that time treating patients with spasticity by electrostimulation of muscles and nerve structures used in psychotherapy, the subcutaneous, epidural location of the electrodes, as well as peroneal implantation (Svozil *et al.* 2015, Kublanov *et al.* 2008). Despite the positive results achieved by the integrated treatment approach, the problem of rehabilitation of children with cerebral palsy in the late residual stage with persistent stereotypes remains unresolved. The problems of restoring muscle control and complex sensorimotor integration (balance, coordination of movement, retention of the body in space) have so far not been

given great attention. Artificial stimulation of the nervous system is one of the most popular ways to activate neural networks in order to activate the brain and initiate neuroplasticity processes (Petrenko *et al.* 2017).

## 2 MATERIALS AND METHODS

### 2.1 Participants

This study involved 6 children with cerebrally palsy, form of spastic diplegia. Patients with intact intellect, no seizures in anamnesis. All children obtained standard treatment, including massage, medical gymnastics with simulators, robotic mechanotherapy, hydrotherapy, and 10 daily sessions of physical therapy, which lasted for 20-25 minutes and neurostimulation of the brain (using the PonS device). Patients underwent functional MRI of the brain before the start of and at the end of the course of treatment using neurostimulation. The patients were aged 8 to 14 years. Patients were evaluated by standard scales GMFSC Scale (gross motor skills), FMS (functional motor scale), Berg balance scale, the Ashworth scale (spasticity). 5 patients with a GMFCS level of development 3 field of the treatment received positive dynamics in FMS.

### 2.2 Neurostimulation

Along with the existing modern high-performance methods of use of peripheral nerve stimulation (Kublanov *et al.* 2017), an innovative method was developed at the University of the state of Wisconsin, USA, in the laboratory, which was headed by renowned scientist Paul Bach-y-Rita, one of the founders of the modern concept of neuroplasticity. An instrument for electrotactile stimulation of human skin, in the most densely innervated tactile region - the tongue, was designed in the laboratory of tactile communication and neurorehabilitation (TCNL) (Danilov *et al.* 2008). Electrotactile stimulation of language is, at the moment, the most effective and safe stimulation of the Central nervous system. Language is the most thin portion relative to the other surfaces of the skin, full of different types of mechano-, thermo - and taste buds, with the addition of free nerve endings. This area has the highest density of mechanoreceptors per unit area and has a minimum two-point discrimination threshold: 0.5-1 mm for mechanical stimulation and 0.25-0.5 mm for electrical stimulation (Danilov *et al.* 2006, Danilov *et al.* 2007). Two major cranial nerves (branch of

trigeminal, 20-22 000 nerve fibers and the facial nerve, 3-6000 nerve fibres) from the anterior surface of the tongue provide the transmission of nerve impulses directly to the structure of the brain stem, activating the complex nuclei of the trigeminal nerve (mesencephalic, sensory and spinal cord-the large core of the trunk) and, at the same time, neighboring nucleus of solitary tract on the branch of the facial nerve is stimulated. The cochlear nuclei are being activated as well, medulla and upper sections of the cervical spine (C2 and C3). The reticular formation of the brain stem, a complex of vestibular nuclei and the ventral part of the cerebellum enters the area of secondary activation (Barbara *et al.* 2009). As is known, the area of the brain stem has a large cluster of neuronal nuclei (N=86), some of them engaged in Autonomous regulation (circulation, respiration), and other sensorimotor integration. One should not exclude possible secondary activation of several common systems of neurochemical regulation of activity of brain nuclei located in the brainstem – noradrenergic, dopamine-mediated error, and acetylcholinergic by dopamine and serotonin. From the same region the trigeminal-spinal path, regulating the activity of spinal motoneurons, goes down solitary-three spinal and Vestibulo-spinal directly involved in the regulation of the activity of the lower limbs and walk (Michelle *et al.* 2009). Intense rhythmic stimulation of active neurons leads to a corresponding activation of synaptic contacts and axon, including the whole complex of pre - and postsynaptic neurochemical mechanisms. Such phenomena as long potentiate or depression of neural networks may underlie the effects observed when using electrotactile stimulation of the tongue. Potentiate long-term (Long-term potentiation, LTP) and long-term depression (Long-term inhibition, LTI), this enhancement/inhibition of synaptic transmission between two neurons that persist long after exposure to the synaptic pathway. LTP is involved in the mechanisms of synaptic plasticity provides the nervous system of a living organism the ability to adapt to changing environmental conditions. Most theorists of neurophysiology believe that long-term potentiate together with long-term depression underlie the cellular mechanisms of learning and memory (Danilov *et al.* 2008).

At the moment, the device for electrotactile stimulation is called PoNS (Portable Neurostimulator), and its use for stimulation of the brain in children with cerebral palsy is a new direction in neurorehabilitation. The matrix, in which are the electrodes of irregular shape; optimized to stimulate the most sensitive areas of language (Fig.1A). The

matrix itself includes 143 electrodes divided into nine 16 - electrode sectors (Fig.1B). Within each sector, only one electrode is active at a given time, the rest are grounded. Stimulation through one electrode occur simultaneously in nine sectors. The electrodes are alternated with a frequency of 50 Hz. The incentive is a triplet of rectangular pulses of microsecond duration.

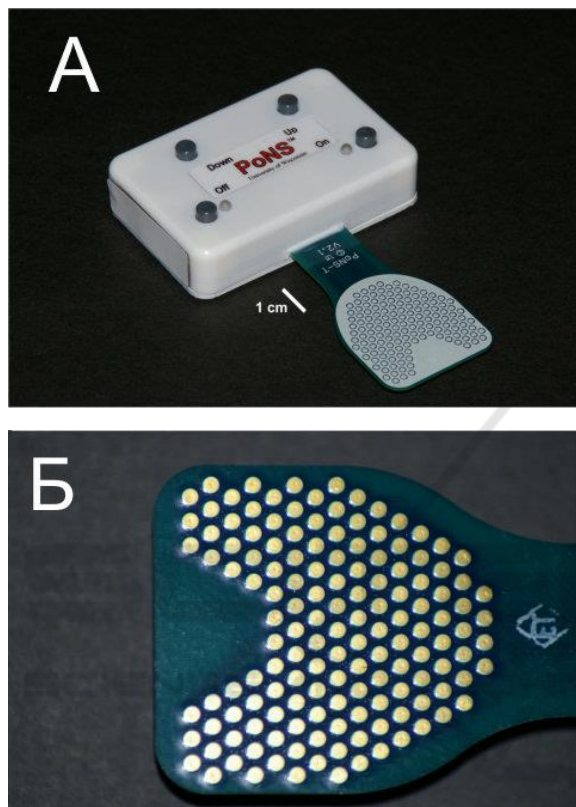


Figure 1: The PoNS device (Portable Neurostimulator). Appearance (A) and close-up of the matrix (B).

Regular stimulation of the PonS device, activating an extensive region of the brain, increases the efficiency of existing neural networks, increases the likelihood of the formation of new synaptic contacts (synaptogenesis), enhances the innate ability of the brain to improve motor functions. The purpose of a successful rehabilitation when such stimulation to restore motor function or to teach new motor skills is done by combining specialized exercises with a wide activation of the brain with the PoNS device.

The studies were conducted in patients with peripheral and Central vestibular disorders (Lomo 2003, Badke *et al.* 2011, Amanda and Raza 2014, Kublanov 2008), multiple sclerosis (Kublanov *et al.* 2010), stroke and ischemic damage (Danilov *et al.* 2015), head injury and spinal cord injury



Figure 2: The PoNS device (Portable Neurostimulator). New design.

(Wildenberg 2011, Wildenberg *et al.* 2013). High effectiveness of peripheral neurostimulation in combination with a specialized physical therapy to restore motor control of the body, balance, walking, speech, eye movements, different aspects of sensorimotor integration was shown. Additional studies, using functional MRI, unambiguously confirmed the presence of a powerful activation of the brain stem and ventral parts of the cerebellum upon stimulation of the tongue, and also the long-term effects of after-effect, the persistence of pockets of activity in the brain of subjects for hours or even days after the last stimulation (Bach-y-Rita 2003, Joseph *et al.* 2011). Additional data analysis showed that while the activation of subcortical structures of the brain are changed and the coefficients of coupling between areas of the cerebral cortex involved in the integrative processes of training (Petrenko *et al.* 2017).

### 2.3 fMRI Data Acquisition and Postprocessing

To investigate the organization of functions, to localize activated cortical areas and to assess the therapeutic effect we used functional magnetic resonance imaging. Conventional T1- and T2-weighted images in three orthogonal planes were obtained also. fMRI was performed on 3.0 T MR-scanner with BOLD (Blood Oxygenation Level Dependent) technique. Functional MR images were acquired using echo-planar imaging (EPI) with repetition time (TR) = 3000 ms, echo time (TE) = 50 ms, flip angle = 90°, field of view (FOV) = 230 mm

and matrix size 128\*128. The research was carried out using active movement functional paradigms for each extremity (both feet and hands) and active count paradigm for patients who could perform these tasks and depending on clinical status, and passive movement or sensory paradigms was performed for those, who could not. Besides, a “virtual walking” paradigm was performed to some patients: they had to imagine they walk. Each activation paradigm lasted 5 minutes with five epochs of movement, 30 seconds each. Taking into consideration patients’ hyperactivity, scanning protocol (number of performed paradigms) could be reduced in some cases to focus on most weak extremity (hand and leg). To obtain high resolution images of whole brain for Talairach coregistration and reslicing along different planes, we used 3D MPRAGE (Magnetization Prepared Rapid Acquisition Gradient Echo) – T1-sequence with the following parameters: repetition time (TR) = 2000 ms, echo time (TE) = 4,38 ms, flip angle = 10°, field of view (FOV) = 250 mm, 160 slices and matrix size 256\*256. Processing of neuroimaging data with the identification of activation sites in each patient and evaluation of the results were carried out using the software package SPM12 (Wellcome Department of Imaging Neuroscience, University College, London, UK) software package running under MATLAB R2011b (The Mathworks, Sherborn, MA, USA) programming. Template space was defined by standard EPI template data in SPM (MNI coordinates - Montreal neurologic Institute, McGill University, Montreal, Canada).

### 3 RESULTS

The first patient before the treatment was able to walk using multisupporting canes within the room, and for longer distances used walkers (500 meters or more), after a course of treatment learned to walk using one cane single-bearing alternator within the room and in school, for longer distances uses a multisupporting cane. The second patient before treatment used multisupporting canes to walk across the room and on the street, could not stand alone without support; the end of the course of treatment learned to walk independently on a level surface (within the room), the patient can stand on his own without support, in school and on the street uses one single-bearing alternator cane. The third patient before the start of treatment used to walk the Walker across the room, at school, and for longer distances used stroller. Upon completion of the course of treatment the patient has mastered multisupporting cane across the room, uses

a Walker in school and can go to the playground, for longer distances use stroller active type. A fourth patient before treatment went using two single-bearing alternator canes within the space and outside, independently and without reliance might stand for a few seconds at the end of the course of treatment learned to walk independently on level surfaces, standing safely alone on the street uses one single-bearing alternator cane. Patient N5 before treatment used multisupporting canes for walking, at the end of treatment mastered walking within the premise of relying on one single-bearing alternator cane, for longer distances uses a multisupporting cane. Patients N6 with the level of development GMFSC 4, before the treatment could move around within the premises using a walker, at school and on the street used active type stroller, at the end of the treatment the patient learned to walk with the use of multisupporting canes within the premises and in school, for longer distances confidently uses a Walker. Also all patients noted decreased muscle tone and improve balance, coordination functions. Improvement of balance, assessed on a scale of Berg, ranged from two to seven units (average 4.5) and as a percentage of the original state improvement was observed from 12 to 70 % (average 31%). (Fig. 3)

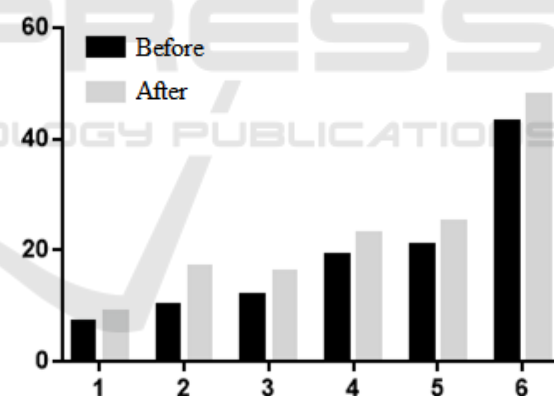


Figure 3: Dynamical differences in patients by Berg balance scale (black – before, grey - after).

According to obtained fMRI data for each subject individually, we detected activations of corresponding areas in response to presentation of movement stimuli, active and passive, located in the hemispheres, before and after neurostimulation.

First patient showed increased activation in right hand motor area, and activation in foot motor area in response to “virtual walking” paradigm after neurostimulation (before it was weaker and appeared in “wrong place”) (Fig.4). Patients N4 and N6 showed significant changes in activation patterns for foot and hand motor areas. All other patients also have had

more expressed activations in response to different stimuli, primarily in foot motor areas and in response to “virtual walking”.

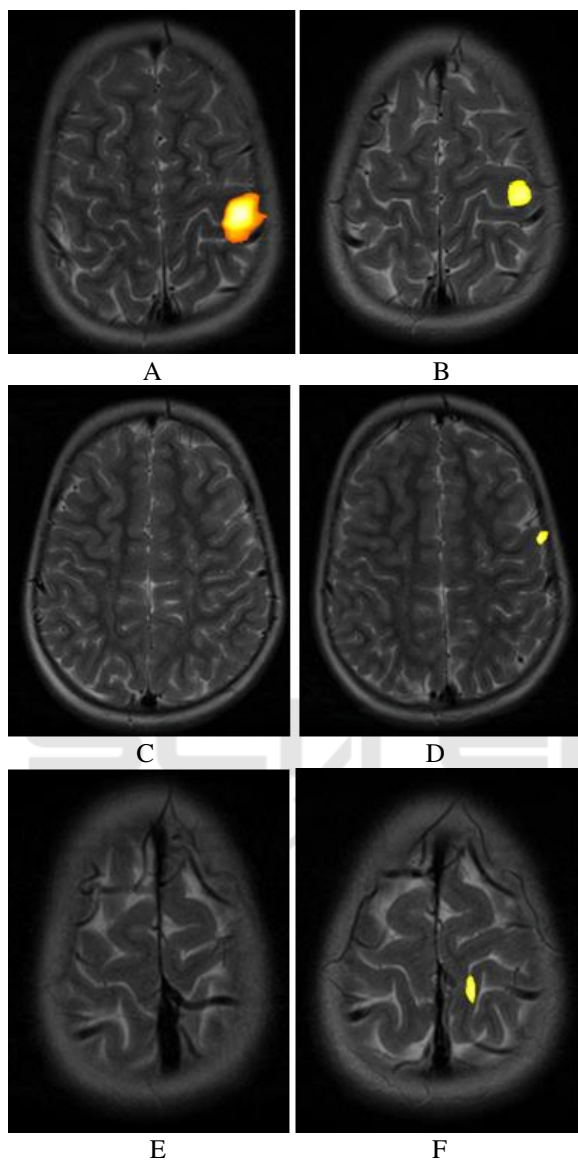


Figure 4: Activation areas in patient N1. A, B – right hand fingers movement, C, D – count paradigm active response, E, F – right leg movement activation, before and after neurostimulation respectively.

#### 4 CONCLUSIONS

Given the limitations and the minimum intensity of the workouts, the main objective of the study was limited by the formation of new motor skills. The patient had to form a new motor skill in 10 sessions,

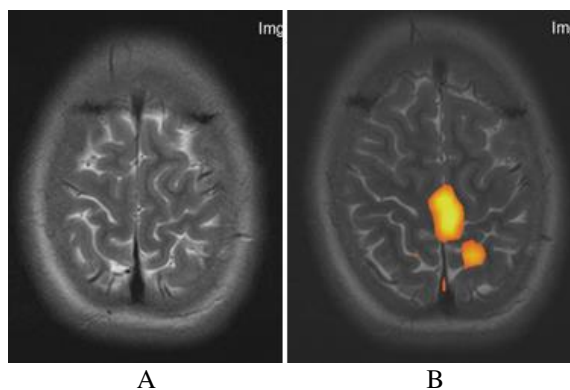


Figure 5: Activation areas in patient N6. Illustration of activation pattern in projection of left leg motor area before (A) and after (B) neurostimulation.

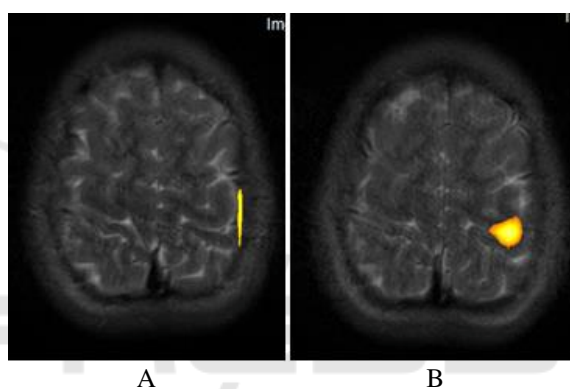


Figure 6: Activation areas in patient N4. Illustration of activation pattern in projection of right hand motor area before (A) and after (B) neurostimulation.

to strengthen it and to confidently use in a daily life. Based on these considerations, it is understandable why overall motor control (scale FMS) statistically significantly improved. Since the task was to develop the skills of motor control, these neural networks improved their functional activity as a result of the neurostimulation. This technique is non-invasive, innovative in the field of neurostimulation, safe and easy to use. Daily 20 minute stimulation of the tongue within two weeks increases the innate ability of the brain to improve motor function, promotes the formation of new motor skills. Neurostimulation with the use of PoNS device, combined with therapeutic exercises (targeted sessions) allows to improve the efficiency of recovery of motor function and motor skills development. Functional MRI active paradigms, with proper and high-quality implementation is an auxiliary method of the objective control of efficiency of treatment.

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