

*Translated from the Russian*

## RESULTS OF THE APPLICATION OF THE METHOD OF TRANSCUTANEOUS ELECTROSTIMULATION OF THE VISUAL SYSTEM IN OPHTHALMOLOGY.

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According to the World Health Organization, in 1972 there were 15 million completely blind people in the world. Unfortunately, two decades later, the number of completely blind people has not decreased, but according to the Royal National Institute of Blindness (U.K.) it has reached 42 million. The number of people who are virtually blind plus those having poor vision is 10 times greater.

According to the data of the well-known Russian ophthalmologist Dr. Fedorov, in the Soviet Union in 1990 there were 840,000 people blind in both eyes, 4.1 million people blind in one eye, 3.2 million people having poor vision in both eyes, and 6.15 million having poor vision in one eye.

The statistical analysis conducted in the Helmholtz Moscow Research Institute of Eye Diseases by Prof. Yuzhakov showed that in 1991 in Russia, there were 400,000 people blind in both eyes, 2.2 million people blind in one eye, 1.7 million people having poor vision in both eyes, and 3 million having poor vision in one eye.

Thus, problems of improving and restoring the damaged visual functions concern many millions of people.

Currently, among the major problems contributing to poor vision and virtual (practical) blindness, there is a leading proportion of severe cases of partial atrophy of the optic nerve (PAON) of various etiologies, and dystrophic diseases of the retina. PAON can have many causes. It can be a hereditary problem, a consequence of different forms of neuritis, glaucoma, degenerative diseases of the optic nerve, or result from various problems that lead to poor blood circulation in the eye and venous stasis, from neurotrauma, compression, etc.

Russian ophthalmologist, Prof. Libman (2) noted that over the last decade, the level of disability related to AON has increased 2 times. A comprehensive examination of 8,000 people with AON showed that 15.1% were totally blind, 39.9% were practically blind, and 45%, with different degrees of poor vision. This means that for 85% of people with AON, there

is a necessity of treatment and a potential to the improvement of vision.

The need for effective treatment is also important because during their disability, one third of these people undergo worsening of the pathological process, and, therefore, a further decrease of visual acuity. According to Prof. Libman, this progressive disability is related to the non-efficiency of traditional methods of treatment. We have observed the same situation with treatment of dystrophic diseases of the retina, in particular, pigment dystrophy of the retina. This is a slow chronic, progressing disease and typical symptoms of this disorder can be seen by the age of 20. In addition to the initial impairments of the night vision, there is gradual narrowing of the visual fields (retinitis pigmentosa?) and it can lead to tunnel vision. Virtual or complete blindness occurs by the age of 40-50.

For many years in the Rostov-on-Don Neurocybernetics Institute, comprehensive research was conducted to design new methods and equipment for improving and restoring impaired visual functions (3,4 and many others).

When the optic system of the retina becomes damaged, there is effective surgery or treatment with optical correction (glasses, contact lenses), or with medication. In many cases, when the disease involves damage of the neurosensory system (neural cells in the retina or the fibers in the optic nerve) we had until recently no effective treatment for improving or restoring vision.

Based on many years of research conducted by leading scientists in Russia, Medical Center for Brain Research in Rochester (NY), the NIH, and the city of Rostov-on-Don, scientists of our Institute developed absolutely new methods for treating these kinds of eye diseases, where traditional methods of treatment (drug or physiotherapy) were useless or poorly effective (5-12).

The essence of these methods for sensor system treatment involves an activation of the peripheral part of the visual system by specially organized electrical currents through an active electrode placed on the closed upper eyelid. The ground electrode should be placed on the inner part of the forearm. The parameters and regimens of such non-invasive transcutaneous electrical stimulation (TES) are different for each patient.

Methods developed at the Neurocybernetics Institute together with the physicians of Rostov-on-Don and Moscow for the treatment of AON, retinal dystrophies, amblyopia and other serious diseases of the visual system, as well as the device created at the Neurocybernetics Institute (ESO-2) were

approved in 1991 in Russia for wide use. It is currently successfully used in more than 700 medical facilities in Russia and other parts of the former USSR. In 1993, Bulgaria has successfully tested the device and it became officially approved for use in this country by the Bulgarian Ministry of Health.

The Neurocybernetics Institute became a training facility for many specialists. More than 1,000 ophthalmologists from Russia and other parts of the former USSR, as well as from India and Jordan have studied and mastered these methods.

The ophthalmologic electrical stimulator (ESO-2) is being used in many medical centers and specialized schools for vision-impaired children throughout Russia.

The ESO-2 device became very effective for treating patients with ophthalmic, neurological and neurosurgical problems involving AON related to glaucoma, neuritis, toxic neuropathy, blood vessel insufficiency, volume process in the optic chiasm area, vision problems related to optochiasmic arachnoiditis, demyelinating diseases, pigmented and macular dystrophy of the retina, amblyopia and myopia of mild and medium grades.

In one paper, we cannot analyze a huge amount of material obtained by ophthalmologists using our method and ESO-2 device. Because of this, we will describe only a few studies mainly conducted in the leading ophthalmic centers.

The study by Prof. Libman (13 years) analyzed the results of our method in 96 patients with different disabling diseases including tapeto-retinal abiotrophy (TRA), PAON, sclerotic macular dystrophy, open angle glaucoma, and anomalies of refraction. Positive effect was achieved in 98% of treated patients. Improvements came in different areas including dynamics of visual acuity and field of vision, as well as electrophysiologic parameters, refractometry data, control of the intraocular pressure (IOP), tonography, etc. In patients with PAON, best results were seen in those who had a vascular-related AON. Treatment also brought results in patients with TRA, both peripheral and central. Moreover, the improvement of visual functions was noted in developed and advanced stages of disease. Very good results were obtained with non-complicated myopia of mild and medium grades. Despite the refractive stability, 80% of patients had their visual acuity significantly improved, and in 51% it reached 1.5 with unchanged correction. Some patients no longer needed glasses.

At the Eye Disease Department of the Medical School of the Russian State

Medical University, the method of TES and the device ESO-2 were used for studies of the influence of TES on visual functions in primary open angle glaucoma patients (14). A course of TES was conducted in 30 patients (26-83 years of age, mean, 67 years), with normal IOP during the treatment period. Mean visual acuity before treatment was 0.63, and after the treatment it was 0.8 (27% increase). In 86% of patients, visual acuity showed improvement. In some cases, this improvement was very significant: from 0.3 to 0.7, from 0.6 to 1.0, from 0.5 to 0.9. Widening of visual fields was seen in 78% of cases. Some patients showed a decrease of the visual field deficit (VFD) by 88% (from 28 to 3 dots), 68% (from 75 to 24 dots). The effect was still visible 5 months after treatment. It should be underlined that a stable effect after TES for up to 6 months was noted in dozens of other publications.

A large number of studies using our method were conducted in the Ufa City (Bashkortostan), in the All-Russia center for plastic eye surgery. Currently, TES has been used in the center for treatment of about 9,000 patients (15-18). Special attention was paid to patients with PAON and pigment TRA with very severe pathology, with visual acuity from "lack of light sensitivity" to "hand motion" and "count fingers". Many electrophysiologic and mathematical criteria (unspecified) were used as prognostic. TES was combined with methods of psychophysiologic correction. Repeated courses of TES with 4-6 months intervals allowed in certain cases, in children with the stated above visual acuity, to form object vision.

In the Samara Medical University, TES (using ESO-2) was used in 198 patients (393 eyes) aged 4-80 years, with different pathologies (19). Positive effect was seen in 191 patients. With accommodation spasm, the vision was restored to 1.0. With mild and moderate myopia, a gain in 1.0-1.5 diopters was achieved and in some cases the glasses were no longer needed.

Increased visual acuity by several tenths (20/20 is 1.0) was seen in hypermetropic astigmatism and accompanying amblyopia. In TRA and macular dystrophy, total fields of vision widened by 120-160 degrees, the scotoma decreased in size, visual acuity improved, for instance, in sclerotic macular dystrophy, from 0.10 to 0.5.

The data from Vladivostok Diagnostic-treatment center show that TES used in 100 patients with PAON resulted in vision improvement in 82.3% of cases, with retinal dystrophy, in 78.9 cases, and with refractive errors, in 81% of cases. In accommodation spasm, the vision is restored to 80-100%,

in progressive myopia, stabilization and decrease of myopia by 0.5-1.0 diopters occurred, in amblyopia, visual acuity improved (20).

In Moscow Ophthalmic clinic an analysis has been performed of the results of TES in 3 groups of patients (21): PAON of different etiology (100 patients), degenerative diseases of the retina (11 patients), traumatic ptoses (19 patients). Initial visual acuity varied from practical blindness to 0.3. The duration of visual impairment varied from 1 month to 20 years. As a result of TES courses, a positive effect was seen in the first group in 73% of cases (73 patients), in the second group, in 54.5% (5 patients), in the third, in 89.5% (17 patients). Depending on the initial value, visual acuity increased from practical blindness to 0.01, from 0.03 to 0.5, from 0.3 to 1.0, visual fields were wider by 10-30 degrees, scotoma disappeared or decreased in size, electrophysiologic parameters improved. If a second course of TES was administered in 4 months, it led to an even further improvement of the visual function.

In a study from Rostov (22), 37 patients (74 eyes) with retinal pigment dystrophy aged from 8 to 59 years have been treated with ESO-2. Genetic analysis showed that the disease was recessive in 44% of patients, dominant in 7%, and sporadic in 49%. In 78% of cases the total field of vision was increased by more than 50%. Visual acuity increased by 0.01-0.09 in 25%, by 0.1-0.15 in 28%, and by 0.2 and more in 21%. If needed, TES was repeated after 3-4 months, which allowed to stabilize the effect.

TES was also effective in treating PAON in neurosurgical patients, as evidenced by a series of papers from the Burdenko Research Institute of Neurosurgery (23-28).

In the reviewed papers, results are presented of the use of TES in the treatment of hundreds of patients from 5 to 65 years of age with AON resulting from cranial-brain trauma and intracranial hypertension of non-tumor origin, following resection of tumors of the chiasmatal-cellar (?) area (pituitary adenomas, craniopharyngiomas, cellar adjacent meningiomas), of the posterior cranial pit, of the inner brain tumors. TES resulted in the increase of visual acuity and widening of the visual fields in about 55% of cases. 22% of these patients were totally blind, 43% had poor vision from light sensitivity to 0.04, 12% with visual acuity 0.05-0.09 and 23%, 0.1 and higher.

None of the totally blind patients (no light sensitivity), like in other papers as well, displayed a positive dynamics. Having this in mind one comes to

conclusion that the efficacy of TES in neurosurgical patients is similar to that of treatment of PAON caused by a wide variety of etiologies. In neuroophthalmic papers, TES efficacy was assessed by registering as improvement of visual functions the appearance of object vision with initial acuity of "hand motion", a twofold increase of acuity when the initial one was less than 10% and an increase by 0.2 with initial acuity higher than 10%. The improvement of visual field was termed positive when the field defects were decreased at least by 15 degrees. TES use in neurosurgical patients was effective in the diseases of various duration (1 month to 10 and more years), as well as in different times after surgery (4).

High efficiency of our method and device in children's ophthalmology is noted in many works of leading Russian ophthalmologists in amblyopia, congenital cataract and glaucoma (after a surgical compensation), posttraumatic and postneuritic PAON (29-34 and others). In ref 29, TES was used in 77 children (8 months to 15 years of age) with PAON. 46 had a hereditary PAON, 5 had a glaucomatous PAON, 15, postneuritic, and 10, posttraumatic. 79% had an improvement of visual acuity. In hereditary PAON, a mean increase was 0.14 (0.03-0.3) in 34 children, in glaucomatous, 0.08 (0.03-0.15) in 4 children, in postneuritic, 0.24 (0.05-0.3), in 14 children, in posttraumatic, 0.3 (0.1-0.5) in 8 children.

In Prof. Khvatova's paper (34), from Helmholtz Moscow Research Institute of Eye Diseases, an analysis was made of the efficacy of TES in treating 56 children after cataract removal. According to the fundal parameters, 3 groups were discerned: 1, without fundal changes; 2, with PAON, and 3, PAON combined with nonpigmented retinal dystrophy or hypoplasia of the fovea. In group 1 patients after TES, visual acuity increased from  $0.88 \pm 0.02$  to  $0.17 \pm 0.04$ , i.e., by 88%. In group 2, the increase was from  $0.096 \pm 0.02$  to  $0.19 \pm 0.03$  (by 50%), and in group 3, from  $0.112 \pm 0.02$  to  $0.197 \pm 0.03$  (by 72%).

The age factor is important in using TES in children's ophthalmology. Nature has made children pretty sturdy. If in animals with a well-developed nervous system the visual system is completely formed within 1 month, children have this system formed by only 15-16 years. Therefore, the sooner the treatment begins, the more efficient it may turn out to be. This is most obvious in amblyopia treatment with TES. In ref 31, 42 children were treated (44 eyes). Group 1 was from 2.5 to 5 years of age, group 2, 5-7 years, group 3, 7-10 years. After the first course of TES, visual acuity in group 1 increased in 79% of cases (mean increase from 0.1 to 0.2), in group 2, in 63% of cases (mean gain from 0.2 to 0.3), in group 3, in 33% of

cases (from 0.2 to 0.3). If groups are selected by the same degree of pathological changes, a significant difference is seen not only between age groups but also in the absolute increase in acuity (35).

Analysis conducted in schools for vision-impaired and blind children only in Russia provides good evidence in favor of the use of our method, which could improve vision in about 50% of the students. This estimate comes also from the distribution of children by pathologies and the degree and level of the damage to the visual system. In schools for the blind, the majority of students have visual acuity in the range of several hundredths, which may be the base for a significant improvement of vision. Without treatment, these children are destined to become practically blind.

The method and the device were effective in asthenopia and in relieving eye strain, prophylaxis and prevention of the occupational diseases in people working as operators (probably dealing with displays all the time), workers at facilities with high eye strain, etc.

In studies of 20 healthy volunteers with normal vision (1.5-2.0) conducted in collaboration with the Y.A. Gagarin Center for Cosmonauts Training, it was established for the first time that TES of the peripheral part of the visual analyzer leads to a significant decrease of the contrast thresholds (36). The parameters of perception of the space frequencies in the low frequency range increased by the average 100%, and in the high, by 10%. Thus, there is a net influence of TES of the peripheral part of the visual system on the parameters of frequency-contrast characteristics of vision.

Results of studies of healthy people with normal vision point to a possibility of using this method not only in disease but also for correction of the functional state of the visual system in normal people, in order to increase the quality of vision during work related to performing important operations and to big professional visual work load.

The results obtained gave reason to widely use TES method in practice. In studies by V.B. Polyansky (37-38) conducted in more than 2,000 patients (computer operators), it was shown that TES courses in asthenopia patients lead to a virtually complete disappearance of symptoms and to a significant improvement of vision. In these patients (asthenopia of different origins), visual acuity were significantly improved (mean, by 0.1-0.2), as well as frequency-contrast characteristics, the accommodation range increased (by 1-2 diopters). In asthenopia exacerbated by mild or moderate myopia, refraction decreased by an average of 0.3 D. Similar results were obtained in the relief of asthenopic symptoms in diamond cutters who have

substantial visual burden (39). These facts open new possibilities for the prevention of asthenopia.

The use of TES in combination with medications and relevant physiotherapy leads to an additional positive effect.

What is the reason for the wide use of the method and device and what are the advantages of our method over other methods of electrical stimulation of the optic nerve?

Currently, several methods have been worked out using direct electrical stimulation of the optic nerve that require a neurosurgical intervention.

First of all, these are works by the Research Institute of Experimental Medicine, Russian Academy of Medical Sciences, and by the Kirov Military-Medical Academy (44). Their method involves a physiotherapeutic electrical stimulation of the optic nerve through electrodes inserted in them during a neurosurgical procedure related to the pathology of the chiasmo-cellar (?) area of the brain (in pituitary adenoma, meningioma of the Turkish saddle, opto-chiasmal arachnoiditis, consequences of the trauma of the skull and brain).

A modification of this method, although not calling for a surgical procedure, also involves insertion of the electrodes in the optic nerves, in this case, transorbitally (45).

A high degree of complexity and high risk of trauma has contributed to the ban on these methods.

At present, another method of electrical stimulation has been worked out in the Center for Eye Microsurgery (46). It consists of placing electrodes for electrical stimulation of the optic nerve by transconjunctival orbitotomy. The stimulation is carried out for 2 weeks and then the electrode is removed. This method is better than the other ones because it does not involve the insertion of the electrodes into the optic nerve. However, it also requires a surgical intervention and makes it impossible to perform additional courses of stimulation, in order to stabilize and increase the therapeutic effect.

Another method, by Fedorov et al. (47) allows for additional treatments. In this method, a miniature device is put in the eye orbit, which is connected to the electrodes on the optic nerve. Using an electromagnetic inducer from the temporal side, distantly in the implanted receiver current pulses can be generated and their parameters can be programmed. This method proved to be effective in treating severe AON. The presence of an implanted receiver made it possible to repeat the procedure. However, the necessity



for implantation of the device and placement of the electrodes on the optic nerve, narrow the scope of use of the device in the everyday practice of health care.

According to present data, in PAON (including severe degree of pathology), part of nonfunctioning nerve fibers of the optic nerve are morphologically intact but are in a state of “parabiosis” and do not conduct excitation (48,49, etc.). Functional capabilities of the other part of the fibers are weakened because of reduced excitability and conductance. Therefore, the first goal is to get the nerve fibers from their “parabiotic” state and to increase excitability and conductance, first of all, of the functioning nerve fibers.

Using our method, this is achieved in the following way. Studies have shown that temporal and nasal positions of the electrode on the eyelid are optimal for the realization of the method. In combination with varying TES parameters, this allows to selectively stimulate specific areas of the retina, and with consequent TES, all its neural apparatus including bipolar and ganglion cells. This enables forming and spreading along the optic nerve fibers (which are axons of the ganglion cells of the retina) of a synchronous shot of neural impulses specific for the nervous system. Thus, in the process of activation of nerve fibers that were before in a “parabiotic” state as a result of a disease process, there is a dominance of a biological component adequate for the nervous system, but not of a physical action as in other methods.

Lasting and positive effect of the non-invasive TES (there is ample clinical evidence to support this) may be explained by following. Improvement and recovery of the visual functions as a result of TES of the peripheral part of the visual system may be based on the reestablishment of conductance of optic nerve that were in a “parabiotic” state, and also on the activation of previously deafferented visual cortex and recovery of its activating and regulatory influence on the function of integrated visual system.

In comprehensive collaborative studies involving the Helmholtz Moscow Research Institute of Eye Diseases, Moscow State University and Neurocybernetics Institute (51 and others), in a series of Ph.D. theses (16, 27, 35, 43 et al.), general principles were found for the reestablishment of functional abilities of the visual system in retinal dystrophies, PAON, in different pathologies of neurosurgical patients, in amblyopia and asthenopia. This corroborates our ideas about the regulatory and normalizing impact of TES on the visual system as a whole.

Periodic repeating of TES courses allows stabilizing the reached state of homeostasis, characteristic of the functioning of the sensory systems in normal conditions.

The regulatory influence of the visual cortex and related subcortical centers can be achieved by the feedback mechanisms existing in the visual system. The encephaloretinal fibers uncovered in experimental and clinical studies are the morphological basis of these feedback mechanisms. According to various authors, centripetal fibers conduct pulse currents from cortex and subcortical visual centers that are regulating the functions of bipolars and other elements of the retina, and the amplitude of the electroretinogram (50).

A reestablishment of the regulatory influence of the higher structures of the visual system can account for the trophic improvement, and therefore, for the improvement of the blood supply when non-invasive TES is used without medications. The same ideas could explain the facts of vision improvement in multiple sclerosis with the optic syndrome possibly resulting from remyelination.

The simplicity of our method, and the possibility of its use without drug therapy make it available for widespread usage (which is now underway) not only in big specialized clinical centers, but also in virtually all ophthalmic, neurosurgical and neurological clinics, in city, district and rural medical facilities, in physiotherapeutic offices, and, in the first place, in medical offices at the workplace, in sanatoria for the blind, in ophthalmic offices in schools for visually impaired, in specialized day care facilities and in groups of people with poor vision.

A non-invasive nature of our method guarantees its complete safety because any intervention-related complications are completely excluded.

Lack of surgical intervention allows one to repeatedly use TES (depending on medical necessity) in necessary intervals (months, years), which would allow for the stabilization and reinforcement of the attained medical effect. It is particularly important in retinal dystrophies.

Along with a medical effect, the method could have a social impact as well because it can help improve vision to many people in a short time. Some people who are in their active years could be brought back to their work. The social effect is also important in what concerns young children, by virtue of the method's lack of pain and safety, compared with invasive methods. This could help social rehabilitation and could substantially decrease a number of students in schools for visually impaired and blind,

mostly by improving vision in hereditary pathologies (PAON, amblyopia).

Non-invasive character and a physiologic nature of the method allow to use it for prevention of occupational diseases related to constant and high visual burden, and to improve of vision quality in professional display operators.