

Original Article

Implantable Closed-Loop System for Restoration of Blinking in Case of Unilateral Facial Nerve Paralysis

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BACKGROUND: In facial nerve (FN) paralysis, a critical task is to restore the orbicularis oculi muscle (OOM) function to prevent corneal atrophy and vision deterioration. In this study, we present the application of a fully implantable bioelectrical closed-loop system for the restoration of blinking in a rabbit model of unilateral FN paralysis. We test the hypothesis that blinking events on the healthy side of a face could be used to trigger an electrical stimulation of eyelid muscles on the impaired side of the face resulting in functional simultaneous blinking.

METHODS: We developed and tested in an animal model a functional prototype of a fully implantable closed-loop device for the restoration of blinking in patients with unilateral FN paralysis. The study was performed on 14 rabbits after complete transection of the FN on 1 side. The animals were divided into 2 groups. In the first group, the subcutaneous electrodes were implanted for functional electrical stimulation of the upper eyelid on the side of the damaged OOM, and the electromyographic signals (EMG) from the healthy OOM were recorded. Two-phase stimulation pulses with adjustable parameters were delivered between electrodes in the medial and lateral corners of a palpebral fissure. Animals from the second group had not received any treatment and were used as a control for facial paralysis.

RESULTS: Stimulation parameters that were sufficient to cause complete eyelid closure were estimated. These parameters included pulse current amplitude, pulse width, and stimulation frequency. We also report the modulation of stimulation parameters during the stimulation period (days 8–30 post transection of the FN). The absence of the eyelid closure in the control group after 1 month of denervation was confirmed.

CONCLUSION: Our study confirmed the possibility of restoration of simultaneous complete eyelid closure by a pre-pain threshold electrical stimulation using a fully implantable closed-loop device in animals with unilateral FN paralysis.

KEYWORDS: Facial nerve paralysis, blinking restoration, blink detection, EMG

INTRODUCTION

Facial nerve (FN) paralysis is the most common among cranial nerve injuries. Due to nerve dysfunction, paralysis of facial muscles develops, and as a consequence—facial deformation and impossibility of eye closure—which can lead to corneal atrophy and loss of vision.^{1,2} In the United States, the incidence of FN paralysis of various etiologies is about 50 cases per 100 000 people.³

Most surgical re-innervations of the facial muscles restore FN functions to the II–III grade level of the House–Brackman grading scale in less than 60% of patients.⁴ Alternative surgical procedures, such as the use of mechanical springs, upper eyelid weights, or muscle transpositions do not provide a complete functional outcome and have high levels of failure and complication.^{4,5,6,7} However, none of these methods, even when used in combination, is fully effective. In a number of studies, some authors point out the effectiveness of functional electrical stimulation after surgery in achieving complete muscle contraction and prevention of atrophy in the denervated facial muscles or denervated limb muscles.^{8–11} Therefore, there is an alternative possibility of eyelid closure caused by direct electrical stimulation of the fully or partially denervated OOM to enhance contraction in partial re-innervation after neurotomy.

Some authors have noted the possibility of complete closure of the palpebral fissure in unilateral FN paralysis caused by direct electrical stimulation in animal models,^{1,2,12-16} as well as the positive effect of electrical stimulation of the denervated OOM on its re-innervation.¹⁷ Various types of stimulation and 2 types of electrodes were evaluated during stimulation with external stimulators.^{1,2,12-16}

Our task was to develop a fully implantable closed-loop device to achieve full simultaneous eye closure. The presence of symmetrical movements on the face means preserving a natural trigger that starts stimulation in the form of EMG signs of blinking on the healthy side in unilateral FN paralysis. After EMG signal analysis and blinking pattern recognition, it is possible to determine blinking time points automatically in real-time. The resulting blinking marker will start the stimulator of the paralyzed muscle, thereby ensuring blinking on the paralyzed side synchronously with the healthy side.

This paper evaluates the effectiveness of the blinking EMG pattern registration system on the healthy side, and the different algorithms of direct electrical stimulation of the denervated OOM. A number of consistent patterns in stimulation have been identified: relation of stimulation current amplitude with pulse width, and temporary changes of it over a 1 month period after FN transection.

These results will contribute to the specification of requirements for permanently implanted devices for the restoration of eyelid closure function.

MATERIALS AND METHODS

In the experiment on 14 mature rabbits, unilateral FN paralysis followed by OOM paralysis was modeled in all animals. In the first group (7 animals), a bipolar registration electrode for EMG recording was implanted in the OOM on the healthy side and a stimulating electrode with 2 contact pads was implanted in the OOM of the facial paralysis side in the upper and lower eyelids, in the lateral and medial corners of the eyes. A master device with an inductive antenna was located on the animal's back. To assess the degree of eye closure, visual analysis of the eye closure was performed during operation with various stimulation parameters. In the second group (7 animals), animals did not receive any treatment after FN transection. These animals were used for control of restoration of movements in OOM on the side of FN paralysis.

FN Dissection and Transection

Before the surgery, animals were anesthetized with intramuscular injections of ketamine (50-80 mg/kg) and xylazine (5-10 mg/kg). The incision was performed between the lower jaw and the base of the auricle, the FN and its branches were identified and then confirmed using stimulation on the FN monitor (Neurosign). After that, complete transection was performed on the main FN trunk with its ligation to prevent possible re-innervation. Bilateral skin incisions were made in the upper eyelids for subcutaneous implantation of petal electrodes to perform stimulation on the paralyzed side and record EMG signals on the healthy side (Figure 1). The electrodes were sutured to the surrounding tissues in the subcutaneous space and the wound was closed with interrupted sutures using 4-0 Vycril. The animals were administered intramuscular antibiotics (penicillin 150 000 IU) for 3 days. Throughout the stimulation follow-up period,

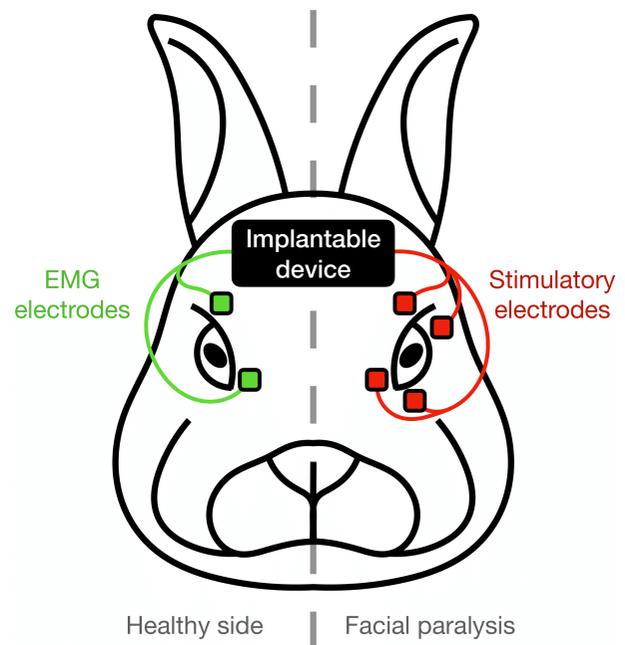


Figure 1. Scheme of electrode location on the head of the experimental animal.

the blinking reflex was checked on both sides to assess OOM innervation dysfunction and to assure the absence of re-innervation.

Implantable System for Blink Restoration

The implantable system for restoration of blinking registers EMG from electrodes on the healthy OOM, detects blinking events in the recorded signal, and performs functional electrical stimulation of the OOM on the paralyzed side with implanted electrodes. A block diagram of the system is shown in Figure 2.

The system consists of:

- implanted electrodes for EMG recording from OOM on the healthy side (Figure 3a);
- a myographic amplifier and analog-to-digital converter designed to enhance and convert the EMG signal;
- a microcontroller, where the EMG signal is digitally processed and control signals are generated to form electric pulses intended to stimulate the current source, which provides amplification of stimulating pulses;
- implantable stimulating electrodes installed in the denervated OOM (Figure 3b);
- an inductive coil which provides an inductive coupling with the external part of the implant and is intended to power the device (Figure 3c); and
- the external part of the system (patient's control) which provides power and control of the implanted part of the electroneurostimulator (Figure 4).

A spirally stranded conductor with biocompatible silicone isolation is used as a movable conductor, connecting the neurostimulator with the electrodes. As electrical pads in contact with a biological medium, petal microelectrodes made of platinum or platinum-iridium alloy are used. Each microelectrode has a hole for fixing an electrode to a muscle.

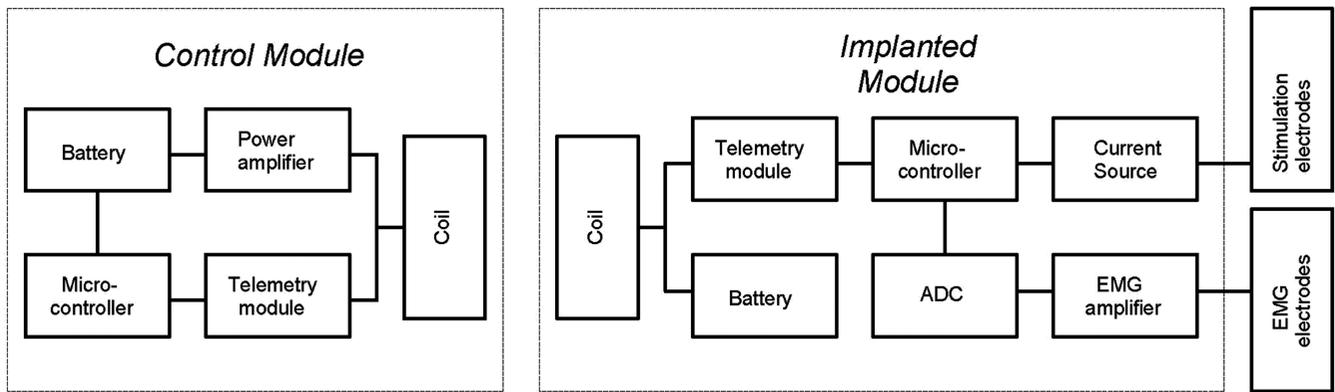


Figure 2. Diagram of the system for restoration of blinking.

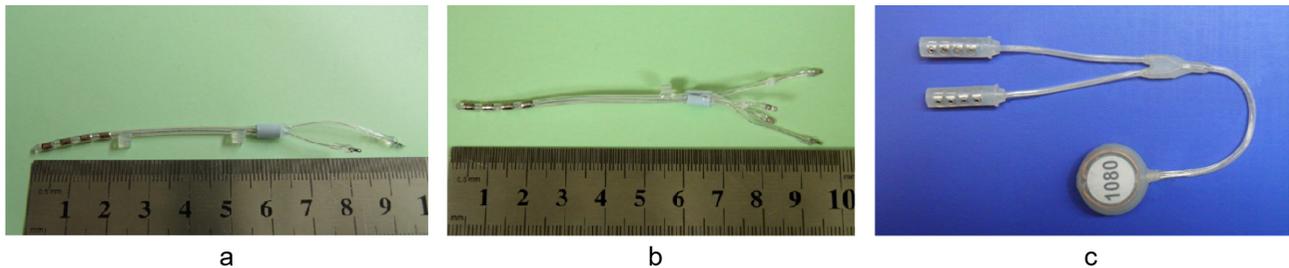


Figure 3. Implantable electroneurostimulator with connectors (c) for recording (a) and stimulating (b) electrodes and an induction coil for communication with an external device.



Figure 4. External control panel with a telemetry antenna.

Blink Detection

The EMG signal was recorded using electrodes implanted in the OOM on the healthy side, and the following processing was then applied (Figure 5).

First, during analog filtration, the normal-mode rejection of the power line noise (50Hz) was performed using a notch filter. Next, filtration using a low-pass filter with a cut-off frequency of 3 kHz was

carried out to remove high-frequency noise in the original signal. This was followed by a uniform sampling with frequency $F_s = 20$ kHz, to digitize the original EMG signal. The digitized EMGs were processed by a microcontroller.

For blink detection, the original signal was passed through 2 digital filters. A high-pass filter was used to get rid of the components which changed at a slower rate than the blink speed and to remove envelope drift. A high-pass filter with Butterworth approximation and a 3-Hz cut-off frequency was used. A low-pass filter with a cut-off frequency of 15 Hz was then applied to remove high-frequency noise components that were not considered informative.

When a filtered EMG signal was obtained, it was squared and averaged in a sliding window to obtain a reference signal. A window length of 500 ms was chosen with a window overlap equal to 10 ms. The average signal was subjected to thresholding, and blinking events were marked as portions where the reference signal was above the threshold. Figure 6 shows an example of blinking events and detection results. The algorithm of blink detection is described in detail in Ref.¹⁸

Electrical Stimulation Protocol

During the experiments, the motor responses of the OOM to electrical stimulation with biphasic current pulses were studied in the animals. The stimulation parameters varied in frequency (40 to 50 Hz), current amplitude (1 to 7 mA), and pulse width (from 100 to 400 microseconds).

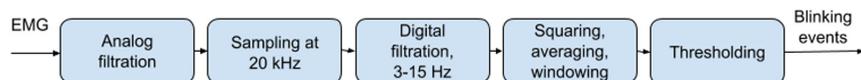


Figure 5. Flowchart of a blink-detection algorithm.

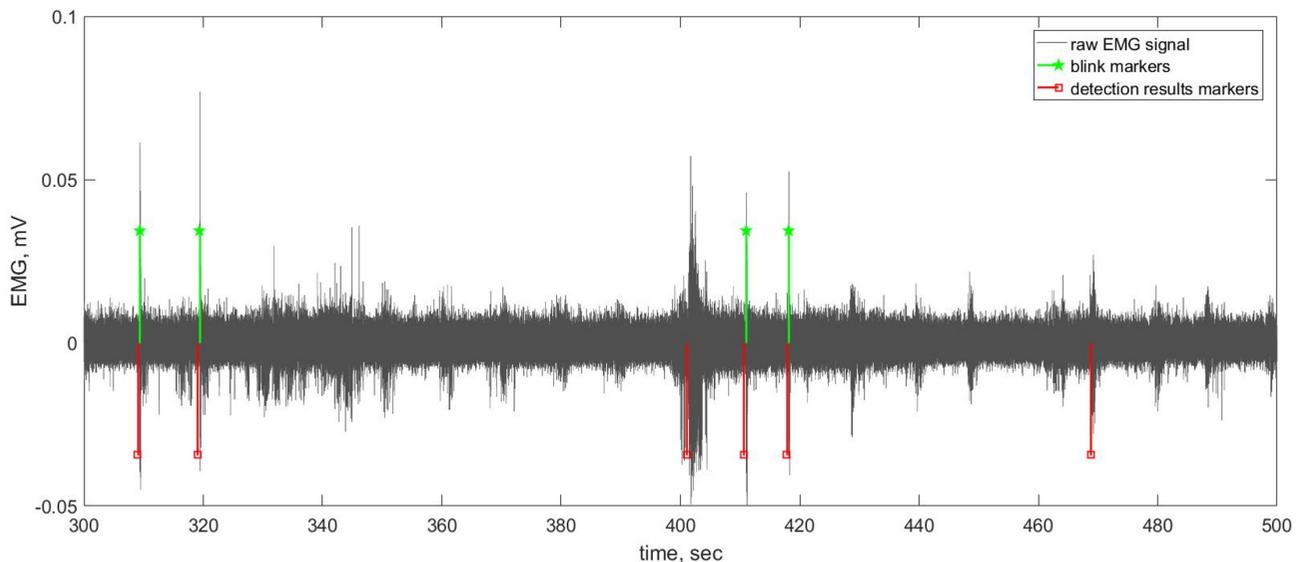


Figure 6. Example of the original EMG signal (gray) with blinking events (marked in green) and blink-detection results (marked in red).

The main objectives of the experiment were to determine the ability of the implantable system to operate in real-time and to determine the parameters of the stimulation effect which achieved full functional OOM contraction without reaching the pain threshold in experimental animals. Particular attention was paid to the achievement of the full functional OOM contraction (palpebral fissure closure) during rehabilitation after complete transection of the FN. The eye closure states were defined as the natural closure without any behavioral deviations of the animal.

Each animal was observed for 30 days. After surgical transection and electrode implantation, animals recovered within 3 days for healing and tissue swelling reduction. Over the next 4 days (4-7 days post-implantation), the animals were subjected to electrical stimulation for 20 minutes every day without registration of the emerging motor responses. This mode can be called "training," as it contributes to the habituation of an animal to the experimental setting and primary muscle adaptation to the direct electrical stimulation.

Starting from the postoperative day 8, each animal was subjected to 2-hour stimulation, and the threshold stimulation current (TSC) values for pulse lengths of 100, 200, 300, and 400 microseconds and frequency of 40, 42, 44, 46, 48, and 50 Hz were estimated. TSC is a minimum strength of the current at which the stimulation achieves a complete palpebral fissure closure. Exceeding the threshold value also led to eye closure, but it could be accompanied by the visible discomfort of an animal. During the experimental procedures, it was observed that stimulation with a pause between stimulation current pulse groups of less than 6 seconds led to degradation of the OOM motor response. Thus, a pause of 7 seconds between stimulation with pulse groups was chosen.

After completion of the stimulation protocol, the rabbits were sacrificed by intracardiac injection of pentobarbital (120 mg/kg), and tissue samples were taken from the upper and lower eyelids of both sides for histological studies. The analysis of these samples is the subject of a separate study.

RESULTS

Surgery

FN identification and the implantation of a myostimulator with electrodes is a simple and easily reproducible surgical procedure. Nerve identification in all cases was performed using an FN monitor and a stimulator. The location of the electrodes was done in the same position in all animals. FN damage was further controlled by registering the absence of a blink reflex on the paralyzed side every 7 days from the start of the experiment. All stages of surgical intervention were completed in all 14 experimental animals. In the control group, no movements were detected in OOM in response to corneal irritation after 1 month of denervation.

Results of the Stimulation Parameters Evaluation Stimulation Current Frequency Effect on TSC Value

In the first part of the experiment, the effect of the stimulation frequency on the value of the TSC was studied. In addition, the order of applied current frequencies and pulse widths was varied in the stimulation protocol to rule out the possibility of carryover effects of the specific current frequency on FN contraction. The dependence of TSC values on time after the FN transection for various frequencies of stimulation currents is shown in Figure 7.

It was determined that the TSC values do not depend on the order of stimulation parameter change (sequence of frequencies and pulse durations in a direct, reverse, or random order). The data presented in Figure 7 illustrate that the TSC values for different pulse frequencies change according to the same pattern. Differences in current strength at different frequencies do not have a specific structure and are likely due to measurement errors. Therefore, further current strength measurements at different frequencies were used to determine an average value of the threshold current value for a specific pulse length on a certain day, assuming that the threshold current strength did not depend on the frequency of the pulses within the range of 40-50 Hz.

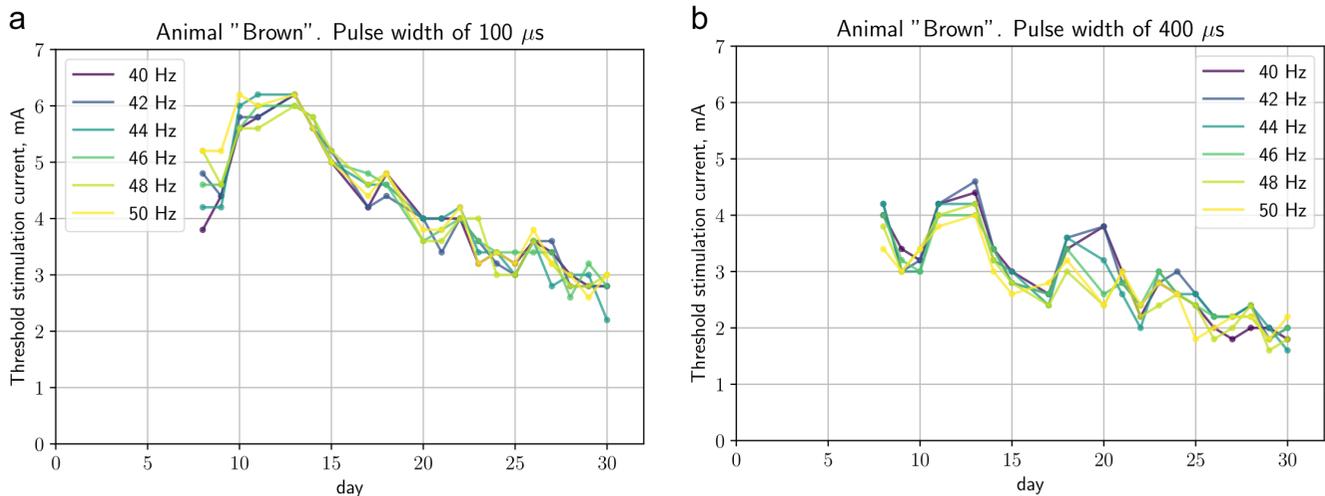


Figure 7. The dependence of TSC on the time after the operation for the animal named “Brown” for different values of stimulation frequency for a pulse width of 100 microseconds (a) and 400 microseconds (b).

Changes of the TSC Over Time After the FN Transection

The experiment was targeted at studying the dependence of a TSC magnitude necessary for eye closure on the time after the operation and the stimulation pulse widths. Figure 8 shows the dependence of the TSC value on time for stimulation pulse widths of 100, 200, 300, and 400 microseconds. Data are shown only for 4 experimental animals, since the remaining 3 animals were subjected to stimulation without recording of TSC values daily (except for time-points of day 14 and day 30 post FN transection).

In addition to the TSC values changing with time after FN transection, the qualities of motor response to stimulation varied as well. Combining the evolution of TSC values over time with observations of motor responses, we can determine 4 characteristic time intervals (phases), which were observed in all animals:

1. The phase of rising TSC value, which was accompanied by poor quality (instability) of motor response. This phase ranged from the beginning of stimulation protocol (day 8) to the second week after FN transection (day 11 for animal “Gray,” day 13 for animals “White” and “Brown,” and day 14 for animal “White JR”).
2. The phase between day 15 and day 20 was characterized by the decrease in the TSC values with apparent stabilization of the motor response: the blink event happened without twitches and tetanic contractions.
3. The phase between days 21 and 30 was characterized by the further steady decline in the TSC values.
4. Toward day 30, rare (≤ 3 per 1 hour of stimulation), sharp, and complete OOM contractions appeared, which could be caused by a partial OOM re-innervation.

Dependence of TSC Value on Pulse Width

Figure 9 illustrates the dependence of the TSC value on pulse width for all animals (N=7), in comparison to day 14 and day 30 after the FN transection. The results show a tendency to a gradual decrease in TS value for higher values of the pulse width. However, during stimulation with a pulse width of 400 microseconds, noticeable activation of surrounding facial muscle tissues was observed, which is suboptimal for the defined task of blink restoration.

DISCUSSION

The results of surgical treatment of patients with FN paralysis ensure the restoration of its functions to the II-III grade level of the House-Brackman grading scale in less than 60% of patients, according to some authors.⁴ In turn, the morphological evaluation of surgical FN re-innervation shows a sufficient, or even hyper, re-innervation of the target muscles.¹⁹⁻²² In our opinion, there are 2 possible explanations for incomplete functional recovery with sufficient muscle re-innervation, one of which is a possible disorder of the established spatiotemporal neuronal patterns of movements from the cortex to the target muscles, due to a long anatomical gap in this neuronal chain. This is confirmed by the positive effect of therapeutic electrical stimulation on functional recovery, synchronous with the natural movement after neurotomy procedures.⁹ This improvement, in turn, can be explained by the restored connection between the central nervous system and target muscles through the newly restored FN due to a blink reflex caused by electrical stimulation, and restored sensation of the muscle function in the central nervous system from the muscle proprioceptors. During electrical stimulation, an actual reinstallation of the facial muscle “driver” occurs in the central nervous system. This is supported by a greater recovery of voluntary movements in patients after neurotomy in combination with therapeutic electrical stimulation, compared to patients without its use during the postoperative period.⁹

The second important aspect is the aberrant terminal re-innervation which may explain unequal involvement of the muscle fibers during excitation, and as a consequence—inefficient motion production.¹⁹⁻²² Permanent use of electrical stimulation in such cases produces synchronization of the muscle excitation and an increase in motion during partial or aberrant muscle re-innervation. In addition, electrical stimulation of denervated muscles causes a reduction in the formation of pathological re-innervations.¹⁷

It should also be noted that a long period of skeletal muscle denervation implies muscle fiber atrophy, and as a consequence, a loss of contractile properties.^{23,24}

In a number of recent studies of permanent therapeutic electrical stimulation in long-lasting muscle denervation, the authors observed

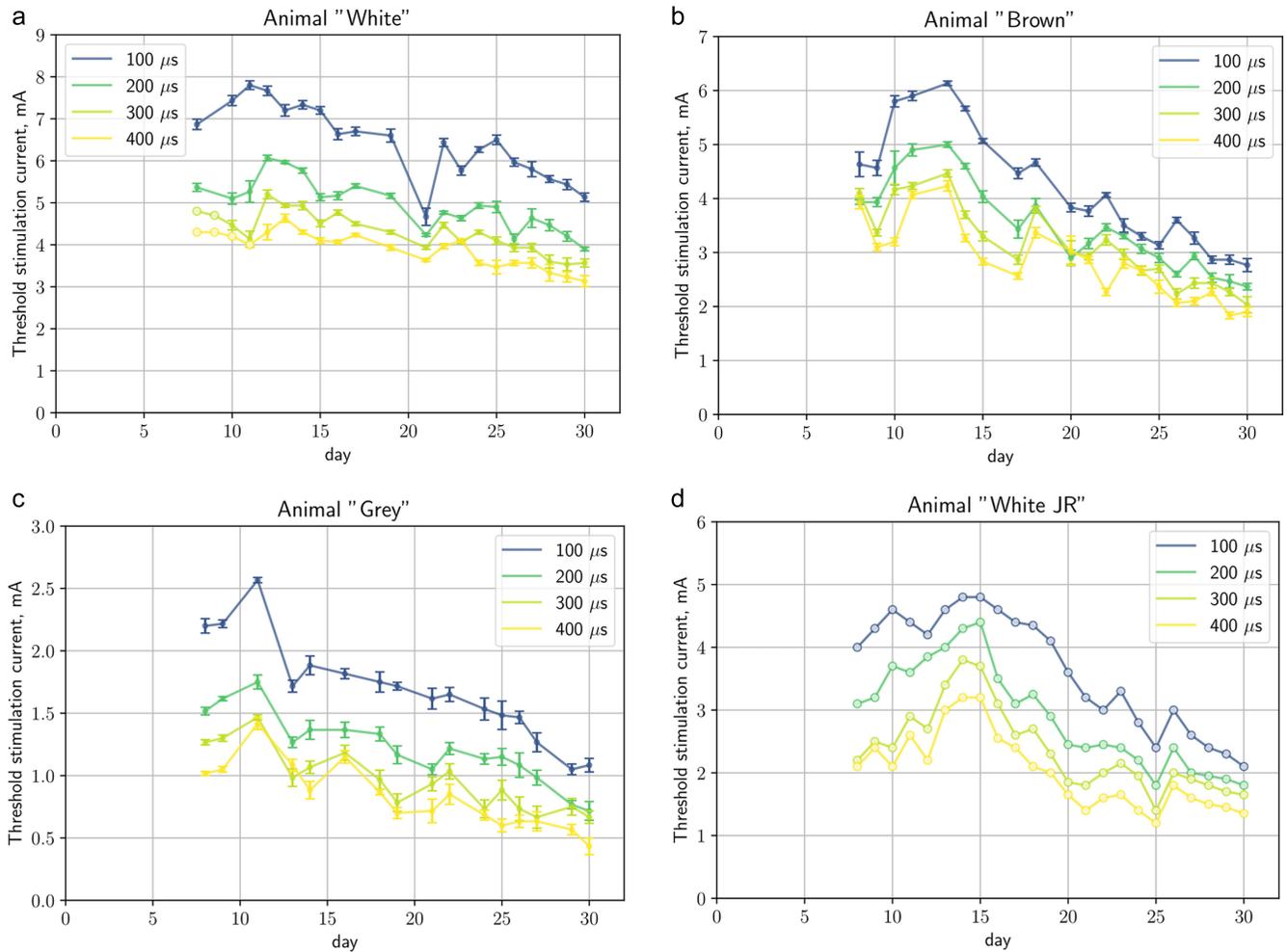


Figure 8. TSC value dependence on time for 4 values of stimulation pulse width in animals named "White" (a), "Brown" (b), "Gray" (c), and "White JR" (d). Filled circles with error bars correspond to mean values and standard error of the mean calculated from values recorded with different pulse frequencies (40, 42, 44, 46, 48, and 50 Hz). Empty circles without error bars correspond to data points, for which only mean TSC value was recorded.

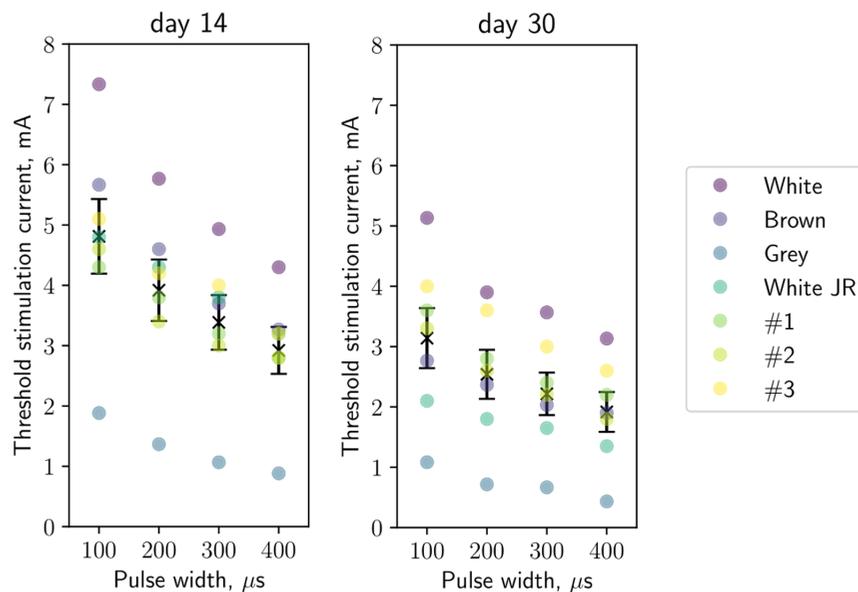


Figure 9. Dependence of TSC value on pulse width illustrated for all animals [N=7] for days 14 (a) and 30 (b) post FN transection. Black crosses with error bars correspond to the mean value and standard error of the mean calculated for specific pulse duration.

the reserves for regeneration and prevention of atrophy in the denervated skeletal muscles, even a few years after denervation.^{9,10}

Therefore, muscle contraction, voluntary or electrically induced, is an effective mechanism for muscle atrophy prevention after denervation.

Consequently, electrical stimulation can be used as a mono-method in FN paralysis when donor nerves cannot be used after the eradication of large tumors of the PCA or jugular foramen, as well as in combination with neurotomy, to prevent muscle atrophy before re-innervation or as a coordinating or enhancing signal in the muscle with incomplete or aberrant re-innervation.

Over the past 50 years, the concept of direct electrical stimulation to restore movement and prevent atrophy in denervated skeletal muscles of the larynx,²⁵ diaphragm,²⁶ and the muscles of the lower extremities²⁷ has been proposed. In a number of studies,^{1,2,12,13,15,16,28} the authors have demonstrated the ability to cause a sufficiently complete OOM contraction by direct electrical stimulation, below the pain threshold, using implantable electrodes and external stimulators at different times after denervation.

The fact that most of the facial movements are symmetrical provides a natural trigger for the start of stimulation in unilateral FN paralysis, and therefore, natural movement synchronization (on the healthy side) with electrically induced ones (on the side with FN paralysis).

EMG registration allows for successful real-time detection of muscle activity. It enables determination of an EMG blinking pattern among other electrical phenomena on the healthy side, and its use as a signal for the start of OOM stimulation on the paralyzed side. Powerful modern microprocessors and sufficient reliability of the inductive power supply (used so far mainly in cochlear implants t.e.) allows the construction of a fully implantable system for the restoration of synchronous blinking in unilateral facial paralysis. Of course, this system can be best used in combination with surgical FN restoration or OOM transposition, which prevents muscle atrophy in permanent myostimulation.

The test results of the proposed implantable closed-loop system in unilateral facial paralysis confirmed the ability to synchronize the blinking on the healthy side and the electrically induced blinking on the side of facial paralysis.

During OOM stimulation, it was noted that the electrode position and shape influenced the value of the current amplitude required for complete eyelid closure. Therefore, the OOM has certain trigger zones, which require a more precise detection for electrode placement. Furthermore, according to Somia,¹⁵ a multi-channel electrode produces more precise muscle excitation which prevents its atrophy, and accordingly, a decrease in muscle strength and stimulation amplitude.

Based on the analysis of previously proposed stimulation parameters and data obtained in this study, it can be concluded that there is a need for their more accurate determination depending on the types of electrodes used and their placement in the optimal OOM

trigger zone, to achieve full eyelid closure with minimal signs of atrophy. The degree of OOM re-innervation during stimulation is also of importance.

The question of the effect of a permanent application of direct electrical stimulation after various neurotomy procedures on the process of muscle fiber re-innervation remains unsolved and is the subject for further study.

CONCLUSION

In this study, we investigated the possibility of using a fully implantable closed-loop system to restore blinking in unilateral facial paralysis. This device ensures complete eyelid closure of the affected side by direct myostimulation, which happens synchronously with the healthy side. In the process of stimulation, the effects, the dependence of the stimulation parameters on eyelid closure during direct stimulation of the denervated OOM, and the optimal stimulation parameters were identified. Biphasic pulse sequences of 300 microseconds at a frequency of 50 Hz effectively caused OOM contractions in all of the rabbits with the denervated OOM. It should be noted that the threshold currents sufficient for complete functional OOM contractions were below the pain threshold, which indicates that this method of stimulation is suitable for use in devices restoring facial muscle functions. Variability in amplitudes of stimulation currents necessary for full OOM contraction is likely to depend on the exact location of electrode implantation. Our further studies will focus on the determination of the most effective location for stimulating electrodes and multi-electrode stimulation. The results obtained in this study are a prerequisite for the clinical testing of the proposed approach and of the devices for the restoration of eyelid closure using electric stimulation in unilateral facial paralysis.

Ethics Committee Approval: All procedures were performed with the approval of the local bioethics committee of Institute of otolaryngology named by prof. A.I.Kolomijchenko according to the National Institutes of Health guidelines (protocol №18/05/2015 3|15).

Informed Consent: Not applicable.

Peer Review: Externally peer-reviewed.

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REFERENCES

1. Salerno GM, Bleicher JN, McBride DM. Restoration of paralyzed orbicularis oculi muscle function by controlled electrical current. *J Invest Surg.* 1991;4(4):445-456. [\[CrossRef\]](#)
2. Salerno GM, McClellan GA, Bleicher JN, Stromberg BV, Cheng SC. Electrical stimulation treatment of dog's denervated orbicularis oculi muscle. *Ann Plast Surg.* 1991;26(5):431-440. [\[CrossRef\]](#)

3. Bleicher JN, Hamiel S, Gengler JS, Antimarino J. A survey of facial paralysis: etiology and incidence. *Ear Nose Throat J.* 1996;75(6):355-358. [\[CrossRef\]](#)
4. May M, Shaitkin BM. The facial nerve. *Thieme P.* 2002.
5. Abell KM, Baker RS, Cowen DE, Porter JD. Efficacy of gold weight implants in facial nerve palsy: quantitative alterations in blinking. *Vision Res.* 1998;38(19):3019-3023. [\[CrossRef\]](#)
6. Kinney SE, Seeley BM, Seeley MZ, Foster JA. Oculoplastic surgical techniques for protection of the eye in facial nerve paralysis. *Am J Otol.* 2000;21(2):275-283. [\[CrossRef\]](#)
7. Lee V, Currie Z, Collin JRO. Ophthalmic management of facial nerve palsy. *Eye (Lond)* 2004;18(12):1225-1234. [\[CrossRef\]](#)
8. Cimbaliyk Y. *Reconstructive Neurosurgical Treatment of Peripheral Nerve Damages Using Long-Term Electrostimulation.* [MD Thesis]. Kyiv; 2014.
9. Gittins J, Martin K, Sheldrick J, Reddy A, Thean L. Electrical stimulation as a therapeutic option to improve eyelid function in chronic facial nerve disorders. *Invest Ophthalmol Vis Sci.* 1999;40(3):547-554.
10. Guo BS, Cheung KK, Yeung SS, Zhang BT, Yeung EW. Electrical stimulation influences satellite cell proliferation and apoptosis in unloading-induced muscle atrophy in mice. *PLOS ONE.* 2012;7(1):e30348. [\[CrossRef\]](#)
11. Tretiyak I. *Diagnosis and Surgical Treatment of Severe Damages of Peripheral Nerves* [MD Thesis]. Kyiv; 2009.
12. Otto RA. Restoration of function in the paralyzed rabbit orbicularis oculi muscle by direct functional electrical stimulation. *Laryngoscope.* 1997;107(1):101-111. [\[CrossRef\]](#)
13. Otto RA, Gaughan RN, Templer JW, Davis WE. Electrical restoration of the blink reflex in experimentally induced facial paralysis. *Ear Nose Throat J.* 1986;65(9):30-2, 37.
14. Sachs NA, Chang EL, Vyas N, Sorensen BN, Weiland JD. Electrical stimulation of the paralyzed orbicularis oculi in rabbit. *IEEE Trans Neural Syst Rehabil Eng.* 2007;15(1):67-75. [\[CrossRef\]](#)
15. Somia NN, Zonnevillje ED, Stremel RW, et al. Multi-channel orbicularis oculi stimulation to restore eye-blink function in facial paralysis. *Microsurgery.* 2001;21(6):264-270. [\[CrossRef\]](#)
16. Tobey DN, Sutton D. Contralaterally elicited electrical stimulation of paralyzed facial muscles. *Otolaryngol Head Neck Surg.* 1978;86:812-818.
17. Willand MP. Electrical stimulation enhances re-innervation after nerve injury. *Eur J Transl Myol - Basic Appl Myol.* 2015;25(4):243-248.
18. Batulin D, Popov A, Bobrov A, Tretiakova A. Eye blink detection for the implantable system for functional restoration of orbicularis oculi muscle. *Jachranka Signal Process Symposium (SPSymo);* vol 2017; 2017:1-4. [\[CrossRef\]](#)
19. Angelov DN, Neiss WF, Gunkel A, et al. Nimodipine-accelerated hypoglossal sprouting prevents the postoperative hyperinnervation of target muscles after hypo glossal-facial anastomosis in the rat. *Restor Neurol Neurosci.* 1997;11(1):109-121. [\[CrossRef\]](#)
20. Morris JH, Hudson AR, Weddell G. A study of degeneration and regeneration in the divided rat sciatic nerve based on electron microscopy - II. The development of the "regenerating unit" *Zeitschrift für Zellforschung und Mikroskopische Anatomie.* 1972;124(2):103-130.
21. Montserrat L, Benito M. Facial synkinesis and aberrant regeneration of facial nerve. *Adv Neurol.* 1988;49:211-224.
22. Shawe GD. On the number of branches formed by regenerating nerve fibres. *Br J Surg.* 1955;42(175):474-488. [\[CrossRef\]](#)
23. Walter JS, Wurster RD, Zhu Q, Laghi F. Respiratory muscle pacing with chronically implanted intramuscular Permaloc electrodes: a feasibility study. *J Rehabil Res Dev.* 2011;48(2):103-114. [\[CrossRef\]](#)
24. Carraro U, Boncompagni S, Gobbo V, et al. Persistent muscle fiber regeneration in long term denervation. Past, present, future. *Eur J Transl Myol.* 2015;25(2):77-92. [\[CrossRef\]](#)
25. Zeale DL, Dedo HH. Control of paralyzed axial muscles by electrical stimulation. *Acta Otolaryngol.* 1977;83(5-6):514-527. [\[CrossRef\]](#)
26. Guo BS, Cheung KK, Yeung SS, Zhang BT, Yeung EW. Electrical stimulation influences satellite cell proliferation and apoptosis in unloading-induced muscle atrophy in mice. *PLOS ONE.* 2012;7(1):e30348. [\[CrossRef\]](#)
27. Liberson WT, Holmquest HJ, Scot D, Dow M. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. *Arch Phys Med Rehabil.* 1961;42:101-105.
28. Rothstein J, Berlinger NT. Electronic reanimation of facial paralysis—A feasibility study. *Otolaryngol Head Neck Surg.* 1986;94(1):82-85. [\[CrossRef\]](#)