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Toward the bionic face: A novel neuroprosthetic device paradigm for facial reanimation comprising neural blockade and functional electrical stimulation

Nate Jowett, MD^{1,2}, Robert E. Kearney, PhD², Christopher J. Knox, BS³, and Tessa A. Hadlock, MD¹

¹ Mass Eye and Ear and Harvard Medical School, Department of Otolaryngology, Surgical Photonics & Engineering Laboratory, 243 Charles St., Boston, USA

² McGill University, Department of Biomedical Engineering, Montreal, QC, Canada

³ Mass Eye and Ear, Department of Otolaryngology, Surgical Photonics & Engineering Laboratory, 243 Charles St., Boston, USA

Abstract

Background: Facial palsy is a devastating condition potentially amenable to rehabilitation by functional electrical stimulation. Herein, a novel paradigm for unilateral facial reanimation via an implantable neuroprosthetic device is proposed and its feasibility demonstrated in a live rodent model. The paradigm comprises use of healthy-side electromyography activity as control inputs to a system whose outputs are neural stimuli to effect symmetric facial displacements. The vexing issue of suppressing undesirable activity resulting from aberrant neural regeneration (i.e., synkinesis) or nerve transfer procedures is addressed using proximal neural blockade.

Methods: Epimysial and nerve cuff electrode arrays were implanted in the faces of Wistar rats. Stimuli were delivered to evoke blinks and whisks of various durations and amplitudes. The dynamic relation between electromyography signals and facial displacements were modelled, and model predictions compared against measured displacements. Optimal parameters to achieve facial nerve blockade by means of high-frequency alternating current were determined, and safety of continuous delivery assessed.

Results: Electrode implantation was well-tolerated. Blinks and whisks of tunable amplitudes and durations were evoked by controlled variation of neural stimuli parameters. Facial displacements predicted from electromyography input modelling matched those observed with a variance-accounted-for exceeding 96%. Effective and reversible facial nerve blockade in awake behaving animals was achieved, without detrimental effect noted from long-term continual use.

Corresponding author: Nate Jowett, MD, Massachusetts Eye and Ear Infirmary and Harvard Medical School, 243 Charles St, Boston, MA 02114, nate_jowett@meei.harvard.edu, Phone: +1 617-573-4193, Fax: +1 617-573-3727.

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Conclusions: Proof-of-principal of rehabilitation of hemifacial palsy by means of a neuroprosthetic device has been demonstrated. The use of proximal neural blockade coupled with distal functional electrical stimulation may have relevance to rehabilitation of other peripheral motor nerve deficits.

Background

Facial palsy is a devastating clinical condition with functional, esthetic, and communication sequelae (1–18), whose ultimate clinical course yields flaccid hemi-facial paralysis (Fig. 1A), post-paralytic facial palsy (Fig. 1B), or combinations thereof. Dynamic reanimation in hemi-facial palsy is principally limited to smile restoration through nerve or functional muscle transfers. Commonly, smile is reanimated using non-emotional trigeminal motor tracts requiring a conscious bite effort that provides volitional but non-spontaneous smile, together with undesired prandial activation. Reanimation outcomes are further limited in that no approach to dynamic restoration of brow elevation, blink, lip pucker, or lower lip movement has achieved consistent success.

Heretofore, the most significant barrier to more effective facial reanimation strategies in both flaccid and post-paralytic facial palsy settings has been a lack of effective control mechanisms for denervated or aberrantly re-innervated facial muscles. Recent technologic advances in signal processing techniques, implantable neural and muscular electrodes, and implantable application specific integrated circuits (ASICs) have led to remarkable breakthroughs in the design and control of prosthetic limbs, devices to restore hearing and other senses, devices to aid gait in the setting of central nervous system disorders, and devices to treat obstructive sleep apnea (19–26). This paper presents a novel implantable neuroprosthetic device (NPD) paradigm for functional electric stimulation (FES) reanimation of the hemi-paretic face (Fig. 2). This paradigm addresses not only the challenge of evoking appropriate facial movements, but also the vexing issue of suppressing undesirable facial activity resulting from aberrant neural regeneration or nerve transfer procedures. The system uses healthy-side electromyography (EMG) signals as the control inputs to a NPD, whose outputs stimulate nerve branches on the paretic side to effect paired muscle contraction (Fig. 3); concurrently applied high-frequency alternating current (HFAC) stimulation provides proximal neural blockade to prevent undesired physiologic muscle activation. Proof-of-principle of this paradigm is demonstrated in a rodent facial nerve model in a series of experiments, whereby implanted nerve cuff electrodes (NCEs) and epimysial electrode arrays (EEAs) are employed to deliver neural stimuli and capture facial muscle EMG activity.

Methods

Overall approach:

A three part series of experiments was performed (Table 1) using a rodent facial nerve model (27–38). Rat blink was used as a surrogate for human blink, while rat whisking (that occurs at different frequencies and amplitudes) was used as a surrogate for continuous proportional control of human facial muscle contractions responsible for movements such as smile or brow elevation. Implanted EEAs were used to record healthy-side facial muscle activity,

while NCEs were used to deliver proximal neural blockade and distal stimulatory signals. Long-term tolerance of implanted electrodes and quality of EMG recordings were assessed, and the capacity to evoke facial displacements of varying amplitudes and durations evaluated. Dynamic relationships between EMG activity recorded from rat facial muscles and facial movements were modeled. Optimal neural blockade signal parameters to prevent synkinetic neuronal discharge while permitting distal branch FES were determined. The safety of continual delivery of HFAC to the facial nerve was assessed over the long-term.

Part 1: Establishment of a Rodent Model for Functional Electrical Stimulation of the Facial Nerve

Head fixation and conditioning:

Ten female Wistar rats, 200–250 g, had titanium head fixation devices (HFDs) implanted and were conditioned to head fixation testing as previously described (28–46). Briefly, rats were trained daily for two weeks to acclimate to handling and restraint. HFDs were then implanted under general anesthesia using ketamine HCl and dexmedetomidine HCl (50 mg/kg; 0.5 mg/kg) via a midline scalp incision. A subperiosteal plane was developed over the calvarium, the sterilized implant secured to the calvarium using titanium screws, and the incision closed in a single layer (Fig. 4A). Daily head restraint training began two weeks later until animals tolerated ten minute-long sessions. A customized resin top-hat enclosure to house the distal ends of electrode leads with their connectors was fabricated and secured to the HFD (Fig. 4B). This enclosure provided protection and ease of access for subsequent recording and stimulation experiments

Electrode implantation:

Once conditioned, electrodes were implanted in the animals during a second procedure under general anesthesia. A 1 cm incision was made in the left cheek and flaps elevated immediately superior to the plane of the facial nerve. In five animals (group 1a), NCEs (custom bipolar design, MicroProbes for Life Sciences, Gaithersburg, MD, Fig. 5, top) were implanted around intact and meticulously dissected zygomatic and buccal branches of the facial nerve. In five other animals (group 1b), blunt dissection was carried deep to the center of the whisker pad musculature for EEA positioning (custom bipolar design, Ripple LLC, Salt Lake City, UT, Fig. 5, bottom) concurrent with NCE placement around the buccal branch of the facial nerve. Electrodes were secured to the deep facial fascia overlying the masseter muscle using 5–0 polypropylene sutures, with leads tunneled in the subcutaneous plane to exit the skin over the occiput. Lead terminals were soldered to a pin connector (A11365–001, Omnetics Connector Corp, Minneapolis, MN) and housed in the customized top-hat enclosure (Figs. 4B and 6).

Quantitative whisker and eyelid displacement recording:

The hardware and software used for monitoring whisking movements was adapted from Bermejo et al (28–33, 47). A single whisker (C-1) on each side of the head was entubulated using a polyacrylamide tube to increase detectability. Whisker displacements were then independently tracked using commercial laser micrometer pairs (MetraLight, Santa Mateo

CA). Blinks were detected using infrared sensors to measure light reflectivity from the cornea and eyelids as described by Thompson et al (48). Computer-controlled air valves were used to deliver corneal air puffs and scented air flows to elicit blink and whisking behavior, respectively.

Evoked stimuli:

While under general anesthesia, animals in Group 1a received varying neural stimuli to zygomatic and buccal branch NCEs, with concurrent tracking of blink and whisker displacements. Animals in Group 1b received neural stimuli to the buccal branch NCE with concurrent capture of whisker pad EMG responses from implanted EEAs. A commercial electrophysiology system (CyberAmp 380 signal conditioner, Digidata 1322A digitizer, pCLAMP 10 software, Molecular Devices, Sunnyvale, CA) combined with analog stimulus isolator units (Analog Stimulus Isolator Model 2200, ADInstruments, Colorado Springs, CO) were used for stimulation and EMG signal acquisition. Neural stimuli comprised trains of current-controlled, charge-balanced square wave pulses (pulse width 0.4 ms, train durations 0.4 ms – 100 ms, repetition rates 1 – 2 Hz, peak-to-peak amplitudes 0.1 – 2 mA). EMG signals were measured with a differential amplifier with pre-filter gain of 10, high-pass filter at 10 Hz, low pass filter at 1000 Hz, notch filter at 60 Hz and post-filter gain of 100. EMG signals were then sampled at 10 kHz with 16-bit resolution, concurrent with whisker and blink displacement signals.

Part 2: Establishing Feasibility of Epimysial EMG as FES Control

Modeling of EMG activity to whisker displacement:

Herein, the healthy-side EMG activity of the whisker pad musculature, as captured using implanted EEAs, were used as inputs and the resulting whisker displacements as the output. Animals from Group 1b above were placed under general anesthesia, and fixed stimuli delivered to the buccal branch NCE (constant current charge balanced square wave, peak-to-peak stimuli 0.5 mA, pulse width 0.4 ms, train width 1.2 ms, repetition rate 1 Hz). The resulting whisker pad EMG responses and C-1 whisker displacements were measured. Methods for Hammerstein system identification described by Jalaieddini and Kearney (49, 50) were used to identify models relating recorded EMG signals to measured whisker displacements in MATLAB (v2015b, The MathWorks Inc, Natick, MA). Muscle was treated as a nonlinear biological system where the relation between neural activation and force was modeled as the cascade of a static nonlinearity followed by a dynamic linear system (51, 52) (Fig. 3, top).

Part 3: Establishing Neural Blockade Effectiveness and Safety

Determination of optimal HFAC parameters and efficacy:

Three animals were implanted with three NCEs on the left buccal branch of the facial nerve, and the animal placed in a laser micrometer field to track evoked whisker displacements. Cathodic pulses from a pulse generator (S88, Grass Instruments, Astro-Med Inc., West Warwick, RI) coupled to stimulus isolators to achieve biphasic constant-current pulses (0.5 mA, 50 μ s pulse width) were delivered to proximal (at 1 Hz) and distal (at 1.5 Hz) NCEs.

High-frequency alternating current (constant-voltage sine wave) was delivered to the central NCE using a function generator (FG085 Kit, JYE Tech, Guilin, Guangxi, China). The peak-to-peak amplitudes (0 – 10 V) and frequency (2 kHz – 40 kHz) were varied to determine optimal blockade parameters. Two further animals, with HFDs implanted and conditioned to head fixation as described above, were implanted with NCEs to the buccal branch and zygomatic branches on the left side. Animals were placed in head fixation for quantitative tracking of awake behavioral whisking, with concurrent application of HFAC and distal FES neural stimuli to generate whisks and blinks.

Establishing safety of continuous HFAC delivery:

Once optimal HFAC parameters were identified, five animals underwent HFD device implantation and restraint training, followed by single bipolar NCE implantation to the buccal branch of the left facial nerve. The marginal-mandibular branch was resected bilaterally to eliminate its contribution to whisking. Beginning one week after NCE implantation, HFAC was delivered continuously for four hours, five days per week, for two weeks (total 40 hours) under general anesthesia. Three minute sessions of awake behavioral whisking assessment were recorded at baseline, after NCE implantation, and preceding each HFAC delivery session. The ratio of the whisking amplitudes between HFAC-blocked and non-blocked sides was tracked for each animal over time.

Results

Part 1: Establishment of a Rodent Model for Functional Electrical Stimulation of the Facial Nerve

Animals tolerated top-hat enclosures and electrode implantations for periods exceeding 40 days prior to scheduled euthanasia, without infection or marked foreign-body reaction despite the subcutaneous exit point of the electrode leads atop the head (**See** Video 1, which demonstrates *Free roaming rat with implanted electrodes*). Electrodes were positioned on facial nerve branches and musculature as demonstrated in Fig 6, with leads tunneled subcutaneously to exit the skin atop the cranium and secured within a resin enclosure bolted to a percutaneous osseointegrated titanium cranial plate (as shown in Fig. 4), available in the “Related Videos” section of the Full-Text article on [PRSJJournal.com](https://www.prsjournal.com) or, for Ovid users, available at INSERT HYPER LINK) (Video Graphic 1). Robust evoked epimysial EMG responses were recorded from the implanted epimysial electrodes, with excellent signal-to-noise ratios (Fig. 7A) throughout this time. Electrical stimulation evoked blinks of varying durations and whisks of varying amplitudes in all NCE implanted animals (Fig. 7B) (**See** Video 2, which demonstrates *Evoked blink and whisk in a live anesthetized rat by means of electrical stimulation of specific facial nerve branches via implanted nerve cuff electrodes*). Nerve cuff electrodes were positioned around intact zygomatic and buccal branches of the facial nerve (as demonstrated in Fig. 6A), available in the “Related Videos” section of the Full-Text article on [PRSJJournal.com](https://www.prsjournal.com) or, for Ovid users, available at INSERT HYPER LINK) (Video Graphic 2).

Part 2: Establishing Feasibility of Epimysial EMG as FES Control

Hammerstein modelling of the relation between epimysial EMG signals (obtained from the undersurface of the whisker pad musculature) to evoked whisk movement demonstrated excellent predictive capacity (Fig. 8), with the model accounting for more than 96% of the variance in whisker displacements.

Part 3: Establishing Neural Blockade Effectiveness and Safety

A 30 kHz sine-wave with a peak-to-peak amplitude of 5V was found to be optimal for inducing blockade of evoked and spontaneous whisking activity in the rat using the customized NCE. In anesthetized animals, this achieved a ~90% reduction in evoked whisking amplitude, without restriction of distal neuromuscular excitability (Fig. 9A, B). In awake animals, a similar reduction in behavioral whisking power was observed between blocked and normal sides (Fig. 9C) (*See Video 3, which demonstrates Neural blockade of physiologic whisking activity in the live awake rat, with concurrent electrical stimulation to evoke blink and whisk via implanted nerve cuff electrodes.* Nerve cuff electrodes were positioned around intact zygomatic and buccal branches of the facial nerve (as demonstrated in Fig 6A). Neural blockade was achieved by delivery of high-frequency alternating current (as demonstrated in Fig. 9B), available in the “Related Videos” section of the Full-Text article on [PRSJJournal.com](https://www.prsjournal.com) or, for Ovid users, available at INSERT HYPER LINK) (Video Graphic 3) with HFAC application. No differences were observed in whisking amplitudes between sides with prolonged unilateral daily delivery of HFAC (Fig. 10). Full results of this series of experiments will be reported in more detail in subsequent publications.

Discussion

While the basic concept of using signals from the contralateral face to drive FES of paralyzed facial muscles has been demonstrated (53–63), prior work has not addressed critical issues relevant to the long-term implementation of this approach. Optimal FES of dysfunctional muscle requires three conditions; muscle must be neurotized, be capable of being stimulated in purposeful and timely fashion, and be devoid of undesirable activity. Neurotization of muscle prevents denervation atrophy and permits FES through neural stimulation without the need for direct muscle stimulation. Though direct muscle stimulation of denervated muscle may prevent atrophy, it requires delivery of high and potentially injurious stimulus amplitudes to evoke contractions (64–66). Such an approach is not feasible in the setting of facial palsy due to excessive power demands on an implanted NPD, coupled with regional nociceptive fiber activation that would result from the delivery of high stimulus amplitudes. In the setting of facial palsy, neurotization of facial muscles may occur spontaneously following neural insult, through interposition graft repair, or through nerve transfer. In cases of long-standing or congenital facial palsy, dynamic facial reanimation may be achieved by functional muscle transfer. Here we propose that muscle contraction be evoked through stimulation of distal native facial nerve branches (or transferred nerves) using electrically-shielded nerve cuff electrodes (NCEs). Such distal facial nerve branches to individual paired-muscles or functional muscle groups of the face are straightforward to access surgically. Likewise, in cases where nerve or muscle transfers are required for

dynamic reanimation, nerve branches to the target muscle are readily accessible for cuff implantation at the time of reanimation surgery or during future re-exploration.

Dynamic reanimation of muscle requires an adequate control signal to effect desired movements at appropriate times. Use of myoelectric activity to reliably drive neuroprostheses has already been demonstrated (67, 68). Herein, we have demonstrated that electromyography (EMG) signals from contralateral, healthy facial muscles may be utilized as control signals to drive FES of the paretic hemi-face. Herein, EMG activity was captured through the use of implanted epimysial electrode arrays (EEAs), obviating the need for external sensors, and a clear mathematical relationship capable of predicting facial displacements from EMG inputs was demonstrated. Use of the contralateral healthy hemi-face for dynamic reanimation of unilateral facial paralysis is a natural choice, as the majority of expressions – especially positive expressions – are symmetric (69). The NPD proposed herein could evoke paired-muscle contraction without a conspicuous phase delay in movement onset between sides. Modern implantable ASICs achieve delays of 5 ms or better on signal receiving and stimulus transmitting arms, with sub-millisecond processing times for most FES applications. When coupled with typical delays on the order of 10 ms for physiologic transduction of the neural stimulus to effect myocyte depolarization, the maximum expected delay between healthy-side detected EMG activity – and subsequent muscular contraction – and paretic-side neural stimulation is on the order of 20 ms, below the ~33 ms threshold above which humans are able to detect asymmetric movement (70, 71).

While stimulation of desirable muscle activity is necessary for functional reanimation, concurrent inhibition of undesirable neural activity is often just as important. No prior work has addressed the vexing issue of how to prevent undesirable muscle activation from aberrantly regenerated axons (i.e. in the case of aberrantly regenerated native facial nerve) or from the normal functioning of transferred cranial nerves (e.g. prandial activation of muscle innervated by transfer of the masseteric branch of the trigeminal nerve). Herein, we describe for the first time the use of concurrent proximal application of high frequency alternating current (HFAC) over prolonged periods to prevent such undesired facial contractions. Delivery of HFAC to peripheral nerve trunks results in reversible induction of localized blockade of propagating action potentials, without impeding distal neuromuscular excitability (72–83); proximal application of HFAC to a motor nerve squelches physiologic activity while maintaining the capacity for distal FES. While there exists brief tetanic onset and offsets responses with HFAC application (72, 75, 84), such repeated responses would be avoided herein through continual proximal delivery of HFAC during waking hours concurrent with distal FES to drive expression. The device could also be implemented in ‘FES-only’ mode to allow physiologic action potentials to pass concurrent with evoked potentials, or ‘neural blockade-only’ mode to induce targeted flaccidity.

In contrast to a recent publication (58), the novelty of the work herein lies in (1) use of clinically-relevant biocompatible epimysial electrodes to capture EMG signals as opposed to transdermal wires, (2) use of clinically-relevant implantable neural cuffs to evoke facial displacements through neural as opposed to direct muscle stimulation via transdermal wires, (3) characterization of a mathematical model capable of predicting whisker displacements from EMG signals as opposed to correlation of signal envelopes, (4) recognition of the

clinically-vexing issue of undesirable physiologic neural activity that occurs with aberrantly innervated muscle, and (5) proposing and demonstrating the long-term efficacy of proximal HFAC application concurrent with distal FES as a solution.

Though the ultimate goal of reanimation is to restore dynamic function of the entire facial musculature, restoration of three symmetric facial movements alone – brow elevation, blink, and smile – would dramatically improve clinical outcomes. Such an approach would require implantation of only three miniature EEAs and NCEs coupled to an implanted ASIC, and would represent a paradigm shift in management. The proposed NPD could also be readily utilized in patients undergoing, *or who have previously undergone successful* trigeminal nerve-driven smile reanimation to re-establish spontaneity. In this realization, smile activation – resulting from the contraction of transferred free functional muscle or native facial musculature driven by the nerve-to-masseter – could be controlled through EMG signals from healthy side zygomaticus major activity through the FES paradigm proposed herein, with elimination of highly undesirable prandial activation through proximal HFAC neural blockade (Fig. 11). Similar to cochlear implant programming, stimulation parameters could be tuned wirelessly as innervation and tissue response to implanted electrodes reach a steady state.

This work has demonstrated the feasibility of employing epimysial EMG signals from healthy-side facial musculature captured using biocompatible and fully-implantable miniature electrodes as a means for control of a FES paradigm to drive reanimation of symmetric expression in hemi-facial palsy. The capacity to effect independent facial movements of varied duration and amplitudes by means of FES of distal facial nerve branches was established. Importantly, the efficacy and safety of proximal neural blockade by means of continuous HFAC delivery as a means to extinguish undesirable facial muscle activity arising from the intrinsic activity of damaged or transferred nerves has been proposed and demonstrated.

The combination of proximal HFAC with distal FES to achieve total extrinsic control over a motor nerve has clinical implications elsewhere where undesirable activity of a peripheral nerve resulting from disease, injury, or nerve transfer exists. Future work will seek to study this paradigm over the long term using a fully implantable miniaturized ASIC currently under development. Beyond FES applications, application of HFAC to peripheral nerves might ultimately prove efficacious for management of spastic disorders and painful neuropathies, as focal blockade of action potential propagation occurs for efferent and afferent pathways (85).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig 1. Hemifacial palsy.

A – Left-sided flaccid facial paralysis, with severe paralytic lagophthalmos, lack of smile, and mid-facial ptosis. B – Left-sided post-paralytic facial nerve syndrome, with severe ocular and mid-facial synkinesis and smile restriction. This condition is the result of aberrant regeneration of the facial nerve following high-grade insult, examples of which include severe Bell's palsy, Lyme disease, Ramsay Hunt syndrome, and extirpation of cerebellopontine angle tumors.

Fig 2. Neuroprosthetic device for hemi-facial reanimation.

Implanted epimysial electrode arrays record EMG signals of healthy side facial musculature, which serve as inputs to an open-loop functional electrical stimulation control algorithm embedded into an application-specific integrated circuit (ASIC), that outputs concordant stimulatory signals to distal nerve branches via implanted nerve cuff electrodes on the diseased side. A constant high-frequency alternating current (HFAC) neural blockade signal is applied proximally on the affected side to prevent undesirable physiologic muscle activation.

Fig 3. Proposed mathematical models for control of a neuroprosthetic device for hemifacial reanimation.

Top – An input EMG signal $g(t)$ is modeled to an output displacement $y(t)$ on the healthy-side of the face using a Hammerstein system. Middle – An input electrical neural stimulus $u(t)$ is modeled to the output displacement $y(t)$ using an NLN structure). Bottom – An input EMG signal from one side of the face is modeled to an output neural stimulus that reproduces the displacement on the contralateral side by coupling the ERS with the inverse of the SRS.

Fig 4. Rat head fixation device (HFD) and electrode lead enclosure.

A – Typical healthy interface of the percutaneous osseointegrated titanium HFD and scalp. *B*

– Top-hat-style resin enclosure secured to the HFD with nuts and bolts (inset: open enclosure demonstrating electrode leads and pin connector).

Fig 5. Electrodes.

Silicone-sheathed nerve cuff with platinum-iridium electrodes (NCE, MicroProbes) (*above*) and a two-channel highly flexible conductive polymer electrode array (CPE, Ripple LLC) (*below*).

Fig 6. Electrode implantation.

A – NCEs are implanted on zygomatic (arrow) and buccal (*) branches of the FN. B – EEAs are implanted underlying the orbicularis oculi (arrow) and whisker pad musculature (arrowhead) under general anesthesia.

Fig 7. Evoked responses.

Evoked EMG response captured using EEAs and elicited blink and whisker response from various neural stimuli delivered using NCEs of the types proposed herein on a live rat model. A – Noise-free differential compound muscle action potentials (CMAP, *bottom*) underlying the whisker pad (electrode spacing of 5 mm, initial gain of 10, sampling rate 10 kHz, AC input-coupled at 10Hz, low-pass filtered at 400 Hz, total gain 1000, stimuli shown above). B – Eyelid response (*top*) to biphasic train stimuli at 1 Hz of constant amplitude and increasing duration demonstrates ability to evoke faster or slower blinks, while whisker response (*bottom*) at 2 Hz stimulus of constant duration and increasing amplitude demonstrates ability to evoke whisks of lesser or greater amplitude.

Fig 8.

Modelling EMG activity to whisker displacement. Top – An impulse response function (IRF) indicates a clear dynamic relationship between an EEA-captured EMG input (implanted underlying the whisker pad) and recorded whisker position. Bottom – The model demonstrated a variance accounted for (VAF) in excess of 96% (*below*).

Fig 9. High-frequency alternating current (HFAC) neural blockade of whisker movement in an anaesthetized and awake rat.

A – Three signals are delivered to the buccal branch of the FN (controls whisking): a proximal stimulation at 1 Hz, HFAC, and a distal stimulation at 1.5 Hz, with parameters as shown in (B). As is seen in (A), HFAC delivery results in a ~90% reduction in whisker amplitude while not affecting the ability to stimulate the nerve distally. B – Stimulation and blockade parameters and NCE positions are shown. C – Constant HFAC is delivered to the left buccal branch using an NCE from $t=30\text{ s}$ to $t=240\text{ s}$ (*above*). Power spectra demonstrate near equal left and right-sided whisking power during the periods immediately before and after HFAC, with a dramatic drop on the left side seen with HFAC (*below*).

Fig 10. Prolonged high-frequency alternating current neural blockade delivery in the rat. Relative maximal whisk amplitudes between left-face (implanted with NCEs on nerve controlling whisking with 4 hours of daily continuous HFAC delivery - see inset) and right-face (normal-side) demonstrate normal or stronger whisker displacements on the side to which HFAC was delivered (green bar approximates normal range).

Fig 11. Proposed paradigm for reanimation of spontaneity of trigeminal nerve-driven smile in the setting of free gracilis transfer.

An implanted epimysial electrode array captures contralateral healthy zygomaticus major EMG activity with leads tunneled subcutaneously to an implanted application-specific integrated circuit (ASIC). Output leads from the ASIC connect to a nerve cuff electrode positioned around the nerve-to-gracilis, which itself is coapted to the nerve-to-masseter. A proximal neural blockade signal is delivered to eliminate undesired prandial activation of the muscle, concurrent with distal functional electrical stimulation signals from the ASIC to reanimate symmetric spontaneous and volitional smile. A similar paradigm could be employed for reanimation of smile spontaneity following nerve-to-masseter transfer to targeted facial branches driving smile (i.e., the “V-VII” transfer, which is indicated in cases where native facial musculature remains receptive to reinnervation).

Video Graphic 1.

See Video 1, which demonstrates *Free roaming rat with implanted electrodes*. Electrodes were positioned on facial nerve branches and musculature as demonstrated in Fig 6, with leads tunneled subcutaneously to exit the skin atop the cranium and secured within a resin enclosure bolted to a percutaneous osseointegrated titanium cranial plate (as shown in Fig. 4), available in the “Related Videos” section of the Full-Text article on PRSJournal.com or, for Ovid users, available at INSERT HYPER LINK.

Video Graphic 2.

See Video 2, which demonstrates *Evoked blink and whisk in a live anesthetized rat by means of electrical stimulation of specific facial nerve branches via implanted nerve cuff electrodes*. Nerve cuff electrodes were positioned around intact zygomatic and buccal branches of the facial nerve (as demonstrated in Fig. 6A), available in the “Related Videos” section of the Full-Text article on [PRSJJournal.com](https://www.prsjournal.com) or, for Ovid users, available at INSERT HYPER LINK.

Video Graphic 3.

See Video 3, which demonstrates *Neural blockade of physiologic whisking activity in the live awake rat, with concurrent electrical stimulation to evoke blink and whisk via implanted nerve cuff electrodes*. Nerve cuff electrodes were positioned around intact zygomatic and buccal branches of the facial nerve (as demonstrated in Fig 6A). Neural blockade was achieved by delivery of high-frequency alternating current (as demonstrated in Fig. 9B), available in the "Related Videos" section of the Full-Text article on [PRSJJournal.com](https://www.prsjournal.com) or, for Ovid users, available at INSERT HYPER LINK.

Table 1.

Live-rodent experiments

Part	Experiment	#
1 – Model establishment	Evoked facial displacements	5
	Evoked EMG	5
2 – Control system	Modelling of EMG to facial displacements	5
3 – Neural blockade	Efficacy	5
	Safety	5