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BRIEF REPORT

Self-Contained Neuromusculoskeletal Arm Prostheses

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SUMMARY

We report the use of a bone-anchored, self-contained robotic arm with both sensory and motor components over 3 to 7 years in four patients after transhumeral amputation. The implant allowed for bidirectional communication between a prosthetic hand and electrodes implanted in the nerves and muscles of the upper arm and was anchored to the humerus through osseointegration, the process in which bone cells attach to an artificial surface without formation of fibrous tissue. Use of the device did not require formal training and depended on the intuitive intent of the user to activate movement and sensory feedback from the prosthesis. Daily use resulted in increasing sensory acuity and effectiveness in work and other activities of daily life. (Funded by the Promobilia Foundation and others.)

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Conventional arm and hand prostheses used after transhumeral amputations are attached to the humerus with a socket that compresses the stump and are moved by native biceps and triceps muscles without somatosensory feedback. Advanced prostheses for the upper arm use motors activated by signals from the patient's remnant biceps and triceps muscles. Patients must learn to contract these muscles to operate a prosthesis that terminates in a robotic hook, gripper, or hand. The devices provide no sensory feedback other than incidental and indirect visual and auditory cues that the patient notes in observing movement of the prosthesis and listening to the activation of electric motors. We developed a self-contained, neuromusculoskeletal prosthetic arm that includes sensory feedback from the surface of a prosthetic hand, allowing for intuitive use of the prosthesis in daily life.

Prosthetic limbs can be anchored in bone at the amputation stump with the use of an implant system that includes two mechanical components[1]: the fixture, a titanium screw that becomes osseointegrated, or incorporated, into the bone, and the abutment, which is placed within the fixture and extends out of the body percutaneously. The prosthesis, which consists of an arm, an elbow joint, and a hand, is connected to the abutment, which transfers the mechanical load to the fixture, which then transfers the load to the bone (Fig. 1B). Mechanical coupling components within the fixture and abutment keep these elements together and seal their interface.

In four patients who had an existing osseointegrated prosthesis with surface electrodes to control a prosthetic hand, we removed the coupling components within the fixture and abutment and replaced them with embedded electrical connectors. The connectors sealed the interface and provided bidirectional communication between the prosthesis and electrodes that we implanted in nerves and muscles, thereby creating a self-contained neuromusculoskeletal human–machine interface

(Fig. 1C). The prostheses were commercially available elbows and hands (the ErgoArm and the SensorHand, both provided by Ottobock, Duderstadt, Germany) that included a custom-designed, embedded electronic system for control and neurostimulation.[2] No other patients at our center have received similar implants.

The regional ethics review board of Gothenburg, Sweden, approved the study, and patients provided written informed consent. Each implanted device, which is called an e-OPRA Implant System, was manufactured by Integrum in Mölndal, Sweden. The study was financed by government grants for collaborative projects between academic centers and industry. There was no industry involvement in the decision to implant the devices, in the collection of study data, or in the writing of this report. The first two authors had confidentiality agreements in place with Integrum. The first author, who worked as a consultant for Integrum with support from government-issued grants, wrote the first draft of the manuscript. All authors reviewed the data, approved the manuscript for publication, and attest to the accuracy and completeness of the data.

METHODS

NERVE TRANSFER FOR PROSTHETIC CONTROL

In preparation for the neuromusculoskeletal interface, three patients underwent nerve transfers to extract neural signals related to the opening and closing of the hand through remnant muscles at the stump.[3] The nerve transfers consisted of rerouting the ulnar nerve to the motor branch of the short head of the biceps muscle and rerouting the deep branch of the radial nerve to the motor branch of the lateral head of the triceps. Neuromas at the ulnar nerve and distal branch of the radial nerve were excised. The distal ends of these nerves were coapted to the ends of motor branches of the musculocutaneous and radial nerves (Fig. 1B). In the fourth patient, natively innervated biceps and triceps muscles were used for prosthetic motor control.

NEUROMUSCULOSKELETAL INTERFACE

In order to extract signals for motor control of the prosthesis, we sutured electrodes onto the epimysium of the two heads of the biceps muscles and the long and lateral heads of the triceps muscles (Fig. 1B).[4] These electrodes, like the surface electrodes used in conventional prostheses, detect signals from the patient's voluntary contraction in remaining muscles to set in motion motors in the prosthetic hand. To obtain sensory feedback, we placed a spiral cuff electrode around the ulnar nerve in all four patients and placed an additional electrode around the median nerve in three patients (Fig. 1B).[5] The cuff electrodes delivered signals for tactile sensory feedback originating from three sensors on the prosthetic thumb through electrical stimulation of the afferent nerve fibers that had been severed in the amputation.

Connection between the implanted electrodes and the prosthesis was achieved by modifying the patients' previously placed osseointegrated implant.[6,7] The existing abutment screw and the central screw (Fig. 1B) were replaced with the current version of the neuromusculoskeletal interface, which contains feed-through connectors that allow wired electrical communication from the distal end of the abutment (outside the body) to the proximal end of the fixture (inside the body). Two leads extend in an intramedullary direction from the proximal end of the fixture and exit transcortically, where they attach to two connectors located outside the bone. From these connectors, leads terminating in the neural or muscular electrodes extend to their respective target nerves and muscles (Fig. 1B). The impedance of the electrodes was monitored over time to assess the functionality of the electrodes and the communication interface.

IMPLEMENTATION

Four to six weeks after surgery, the patients were fitted with self-contained arm prostheses that required no external batteries, wires, or equipment in order to function and that were controlled by the epimysial electrodes. In January 2017 (one patient) and September 2018 (two patients), electrical stimulation intended to elicit tactile perception was coupled to force sensors in the thumb of the prosthetic hand, providing graded sensory feedback during grasping of common objects. The fourth patient did not participate in follow-up after the initial fitting of the prosthesis and was therefore not provided with sensory feedback.

Functional prosthetic control was assessed through evaluation of the precision with which

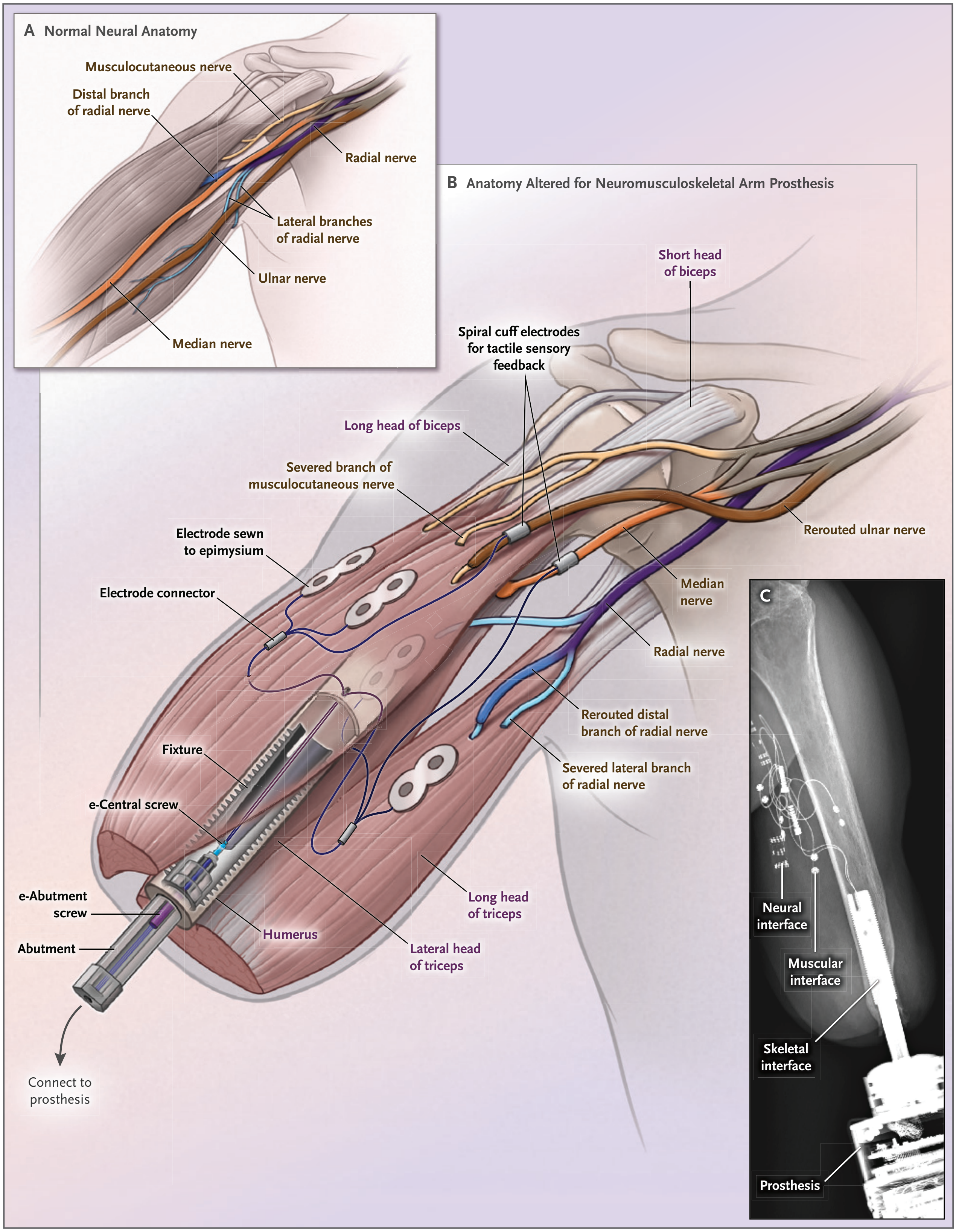
A Normal Neural Anatomy
Musculocutaneous nerve
Distal branch of radial nerve
Radial nerve
Lateral branches of radial nerve
Ulnar nerve
Median nerve
B Anatomy Altered for Neuromusculoskeletal Arm Prosthesis
Short head of biceps
Spiral cuff electrodes for tactile sensory feedback
Long head of biceps
Severed branch of musculocutaneous nerve
Electrode sewn to epimysium
Electrode connector
Rerouted ulnar nerve
Median nerve
Radial nerve
Rerouted distal branch of radial nerve
Severed lateral branch of radial nerve
Fixture
e-Central screw
e-Abutment screw
Abutment
Humerus
Long head of triceps
Lateral head of triceps
Connect to prosthesis
C
Neural interface
Muscular interface
Skeletal interface
Prosthesis

Figure 1 (facing page). Neuromusculoskeletal Arm Prosthesis with Targeted Muscle Reinnervation.

Normal neural anatomy is shown in Panel A. Panel B depicts surgical nerve transfer, muscular and neural electrode placement, and the osseointegrated implantation system for skeletal attachment (abutment and fixture) and bidirectional communication to the external prosthesis (e-abutment screw, e-central screw, and electrode connectors, with "e" denoting electrical feedthrough). Unlike earlier devices, "e-devices" allow direct communication between a prosthetic hand and electrodes implanted in the nerves and muscles of the upper arm. Panel C is a radiographic image of the neuromusculoskeletal prosthesis indicating the neural, muscular, and skeletal interfaces.

patients could operate their prosthesis in two tasks: the minimum increment of force that could be applied to an object by the prosthetic hand during closing (grasping force) and the minimum incremental activation of the hand during opening and closing movements (displacement). These evaluations were performed when the prosthetic hand was controlled through surface electrodes (before surgery) and again when controlled by epimysial electrodes (1 month after the prosthetic fitting). In addition, the signal-to-noise ratio of these two sources of control was measured at maximum voluntary contraction before and after incorporation of the epimysial electrodes. Sensory acuity was measured with the use of psychometric tests. For details, see the Supplementary Appendix, available with the full text of this article at NEJM.org.

PATIENTS

Patient 1 is a right-handed 47-year-old man who had desmoid fibromatosis in his right forearm. In 2003, despite multiple excisional surgeries and radiotherapy, he required a transhumeral amputation that left 26 cm of humeral bone. He initially received an electrically driven prosthesis that was attached to the body with a socket that kept the prosthesis in place through the constant application of pressure on the stump. He wore the prosthesis sporadically owing to discomfort caused by the socket. The socket attachment was replaced by an osseointegrated prosthetic implant in 2009, with surface electrodes used to control the prosthesis. The patient had difficulty operating his prosthetic hand with the conventional skin-surface electrodes because it became unresponsive when he was outdoors. He lives in a cold Nordic climate, where he works outdoors as an operator of heavy-duty vehicles. Temperature affects the capabilities of electrodes on the surface of the skin to record myoelectric signals, particularly as the skin becomes dry. He also reported "distressing" phantom limb pain with an intensity of 6 on a 10-point visual analogue pain scale on which 0 indicates no pain and 10 the worst possible pain. In January 2013, when he was 41 years old, he underwent implantation of the neuromusculoskeletal interface. The patient's prosthetic control with the use of the implanted electrodes in daily life was reported in a publication in 2014.[8]

Patient 2 is a right-handed 46-year-old man who lost his left arm as a result of high-voltage electrocution in 2011 while working as electrician. He initially used an electrically driven prosthesis that was attached to his body with a socket and controlled by surface electrodes. He had back pain and discomfort that made it difficult to control the prosthesis. In 2014, he received an osseointegrated implant to allow skeletal attachment of the prosthesis. The mechanical discomfort related to prosthetic attachment resolved, but the patient reported poor control of the prosthetic hand and preferred to use a prosthetic "gripper," which he found to be more useful during manual work. In January 2017, when he was 44 years old, he had nerve transfers and underwent implantation of the neuromusculoskeletal interface.

Patient 3 is a right-handed 44-year-old man who had traumatic loss of his right arm in 1997 during an accident while working on an oil platform. He had worn an electric prosthesis with a socket attachment sporadically for 5 years but abandoned it owing to discomfort and poor functionality. In 2013, he reported increasing back pain resulting from the postural imbalance produced by the missing arm. In 2014, he received an osseointegrated implant for skeletal attachment of the prosthesis and began using an electric hand controlled with surface electrodes, but he reported poor control over the prosthesis. He also reported phantom limb pain, which he described as "stabbing" and "cramping," with an intensity of 3 on a 10-point visual analogue pain scale. In January 2017, when he was 42 years old, he underwent nerve transfers and received an implant with the neuromusculoskeletal interface.

A video showing use of prostheses in daily life is available at NEJM.org

Patient 4 is a left-handed 44-year-old man who had a traumatic amputation of his left arm while using a rolling machine at work in 2003. He wore a prosthetic hand sporadically owing to discomfort caused by the socket used for attachment and to poor function related to the surface electrodes used to control the hand prosthesis. In 2007, he received an osseointegrated implant for direct skeletal attachment of his prosthesis, a procedure that resolved the discomfort caused by the previous socket attachment. In May 2017, at the age of 42 years, he underwent nerve transfers and implantation of the neuromusculoskeletal interface.

RESULTS

All patients used signals acquired by the implanted epimysial electrodes as the source of control for their prostheses in daily life (see Fig. 2; and Video, available with the full text of this article at NEJM.org). Because the patients were familiar with the operation of a prosthetic hand with surface electrodes, they did not re-

Figure 2. Neuromusculoskeletal Arm Prosthesis Used Unsupervised in Daily Life.
Shown are images of Patient 1 (Panels A and B), Patient 2 (Panels C, D, and E), and Patient 3 (Panels F, G, H, and I).

quire training to use the neuromusculoskeletal interface. Myoelectric activity, recorded by the epimysial electrodes on the reinnervated muscles in Patients 2 and 3, was observed at the first follow-up, 4 weeks after surgery, and increased in amplitude over time.[9] Operation of the prosthetic hand was switched to these intuitive control signals between 10 and 40 weeks after surgery. Precision in prosthetic control improved in all patients (for quantitative results, see Fig. S1B, S1C, and S1D in the Supplementary Appendix). Patient 4 did not participate in follow-up but had documented use of his neuromusculoskeletal prosthesis in daily life for 2 years 6 months.

Sensations elicited through direct nerve stimulation were referred to the phantom hand in all patients (Fig. S1E). The sensations were described as being similar to a "touch by the tip of a pen" and gradually acquired a more "electric" character at higher intensity, with increased pulse frequency.[10] Initially, patients could perceive a difference in the intensity of sensations when the frequency of stimulation was increased or reduced by 50% (Fig. S1F and S1G). After a month of daily use of sensory feedback, a change of approximately 30% in the frequency of stimulation could be perceived as an increase or decrease in intensity of tactile sensation.

No serious adverse events, infections, bleeding, or discontinuation of use of the prosthesis due to adverse events occurred as a result of the implants (Table S2). The neuromusculoskeletal interface remained functional after 3 to 7 years of use in all three patients who could be followed. Electrode impedance increased for approximately 5 months after implantation and then remained relatively stable (Fig. S1A). Patients 1 and 3 had complete relief of phantom limb pain. Patient 2 had not had phantom limb pain before the intervention. Patient 1 has become employed full-time as a result of the improved functionality of the prosthesis, which has also allowed him to ski, go ice fishing, and ride a snowmobile. The preferred terminal device of Patient 2 became a myoelectric hand rather than a gripper owing to the superior control provided by the implanted electrodes. He has been able to engage in rally-car racing and to repair cars with his neuromusculoskeletal prosthesis. Patient 3 has been able to orienteer, canoe, and ski while using his neuromusculoskeletal prosthesis. All patients reported having greater trust in their prosthesis since the intervention, referred to it as being part of themselves, and reported positive effects on their self-esteem, self-image, and social relations, although these statements were not assessed with any established measure.

DISCUSSION

We report the effects of the implantation of neural and muscular electrodes to provide control and somatosensory feedback to an osseointegrated arm prosthesis in four patients, three of whom had clinical follow-up. The prosthesis was effective during the performance of activities of daily living without supervision and allowed intuitive somatosensory feedback, thereby requiring no formal training. The procedure augmented the performance of previously implanted osseointegrated prostheses in these patients. In the future, the new osseointegrated interface will incorporate other types of neuromuscular electrodes, potentially allowing for the use of more sophisticated neural interfaces.

There are a limited number of reports on the long-term implantation of electrodes that provide somatosensory feedback, and these reports have been confined to controlled research environments.[11,12] An exception is a study in two patients who for up to 13 days wore prostheses controlled by conventional surface electrodes that allowed tactile feedback enabled by a neural electrode through percutaneous leads.[13] One of these patients later used the same system for 49 days.[14] These patients reported improvement in the performance of daily activities despite wearing the prosthesis for a limited time each day, providing support for our findings that implanted electrodes can be used for prosthetic control[15,16] and sensory feedback.[17-20]

The major challenge in enabling sensory feedback in an artificial limb is creating a neural interface that conveys a high amount of sensory information to the nervous system in a way that is perceived effortlessly by the user. Ideally, the number of sensors in the prosthetic hand would match the resolution of the interface, so the patient would have feeling in all the locations on the artificial hand where the sensors are capable of detection. The relevance of the work presented here is not in the number of perceived and measured sensations but in the achievement of an integrated and fully self-contained prosthesis with implanted electrodes that can be used reliably in daily life, enabling intuitive control and somatosensory feedback of the hand.

In conclusion, we report outcomes for four patients after transhumeral amputation, who received a neuromusculoskeletal prosthesis that allowed intuitive and unsupervised daily use over several years.

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REFERENCES

1. Thesleff A, Brånemark R, Håkansson B, Ortiz-Catalan M. Biomechanical characterisation of bone-anchored implant systems for amputation limb prostheses: a systematic review. Ann Biomed Eng 2018;46:377-91.
2. Mastinu E, Doguet P, Botquin Y, Hakansson B, Ortiz-Catalan M. Embedded system for prosthetic control using implanted neuromuscular interfaces accessed via an osseointegrated implant. IEEE Trans Biomed Circuits Syst 2017;11:867-77.
3. Kuiken TA, Li G, Lock BA, et al. Targeted muscle reinnervation for real-time myoelectric control of multifunction artificial arms. JAMA 2009;301:619-28.
4. Ortiz-Catalan M, Brånemark R, Håkansson B, Delbeke J. On the viability of implantable electrodes for the natural control of artificial limbs: review and discussion. Biomed Eng Online 2012;11:33.
5. Pasluosta C, Kiele P, Stieglitz T. Paradigms for restoration of somatosensory feedback via stimulation of the peripheral nervous system. Clin Neurophysiol 2018;129:851-62.
6. Brånemark R, Brånemark P-I, Rydevik B, Myers RR. Osseointegration in skeletal reconstruction and rehabilitation: a review. J Rehabil Res Dev 2001;38:175-81.
7. Jönsson S, Caine-Winterberger K, Brånemark R. Osseointegration amputation prostheses on the upper limbs: methods, prosthetics and rehabilitation. Prosthet Orthot Int 2011;35:190-200.
8. Ortiz-Catalan M, Håkansson B, Brånemark R. An osseointegrated human-machine gateway for long-term sensory feedback and motor control of artificial limbs. Sci Transl Med 2014;6(257):257re6.
9. Mastinu E, Branemark R, Aszmann O, Ortiz-Catalan M. Myoelectric signals and pattern recognition from implanted electrodes in two TMR subjects with an osseointegrated communication interface. In: Programs and abstracts of the 2018 40th Annual International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC), Honolulu, July 17–21, 2018:5174-7.
10. Ortiz-Catalan M, Wessberg J, Mastinu E, Naber A, Brenemark R. Patterned stimulation of peripheral nerves produces natural sensations with regards to location but not quality. IEEE Trans Med Robot Bionics 2019;1:199-203.
11. Petrini FM, Valle G, Strauss I, et al. Six-month assessment of a hand prosthesis with intraneural tactile feedback. Ann Neurol 2019;85:137-54.
12. George JA, Kluger DT, Davis TS, et al. Biomimetic sensory feedback through peripheral nerve stimulation improves dexterous use of a bionic hand. Sci Robot 2019;4(32):eaax2352.
13. Graczyk EL, Resnik L, Schiefer MA, Schmitt MS, Tyler DJ. Home use of a neural-connected sensory prosthesis provides the functional and psychosocial experience of having a hand again. Sci Rep 2018;8:9866.
14. Cuberovic I, Gill A, Resnik LJ, Tyler DJ, Graczyk EL. Learning of artificial sensation through long-term home use of a sensory-enabled prosthesis. Front Neurosci 2019;13:853.
15. Salminger S, Sturma A, Hofer C, et al. Long-term implant of intramuscular sensors and nerve transfers for wireless control of robotic arms in above-elbow amputees. Sci Robot 2019;4(32):eaaw6306.
16. Mastinu E, Clemente F, Sassu P, et al. Grip control and motor coordination with implanted and surface electrodes while grasping with an osseointegrated prosthetic hand. J Neuroeng Rehabil 2019;16:49.
17. Schiefer MA, Graczyk EL, Sidik SM, Tan DW, Tyler DJ. Artificial tactile and proprioceptive feedback improves performance and confidence on object identification tasks. PLoS One 2018;13(12):e0207659.
18. Zollo L, Di Pino G, Ciancio AL, et al. Restoring tactile sensations via neural interfaces for real-time force-and-slippage closed-loop control of bionic hands. Sci Robot 2019;4(27):eaau9924.
19. Page DM, George JA, Kluger DT, et al. Motor control and sensory feedback enhance prosthesis embodiment and reduce phantom pain after long-term hand amputation. Front Hum Neurosci 2018;12:352.
20. Clemente F, Valle G, Controzzi M, et al. Intraneural sensory feedback restores grip force control and motor coordination while using a prosthetic hand. J Neural Eng 2019;16:026034.