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A neuromuscular platform to extract electrophysiological signals from lesioned nerves: A technical note

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Abstract—The volitional control of prosthetic devices could be greatly enhanced if the information formerly supplied by peripheral nerves to the amputated limb could be utilized. So that practical access to this information could be gained, a method was established to form a stable biological interface with fascicles of lesioned nerves. A small strip of an intact muscle was isolated in rats with the use of a silicone tube cuff electrode and innervated by the lesioned peroneal branch of the sciatic nerve. After 4 weeks survival, stimulation of the nerve fascicle produced reliable signals from the neuromuscular platform in the range of 0.5 to 2.0 mV. Histologically, myotubes remained intact and axons could be identified growing in and over the surfaces of the isolated muscle strips. These or similar interface techniques may supply electrophysiological signals of sufficient amplitude and reliability to provide peripheral nerve-based guidance information for prosthetic devices.

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INTRODUCTION

The volitional operation of prosthetic devices requires some source of information that can be utilized for guidance according to the operator's wishes. While amputation removes the structural elements of the limb, the ends of lesioned nerves remain and continue to carry information for the operation of muscles and sensory information from the removed limb (1). It has been shown that lesioned peripheral nerves that are not permitted to regenerate continue to demonstrate a normal pattern of discharge appropriate for the muscles that they originally innervated for extended periods of time (1). Attempts to use lesioned nerves as a source of information for prosthetic devices in human amputees have met with limited success (2). Part of the difficulty in the use of signals derived from motor nerves is their low amplitude. The signals obtained from even normal nerves via nerve cuff electrodes during functional activity are in the range of 10–50 μV (3). While signals of this amplitude

can be used for prosthetic devices (4), the signal level obtained from lesioned nerves is complicated by a progressive attenuation with time after injury (5). The attenuation of nerve discharge amplitude or nerve action potentials originates in part from a slow atrophy and/or loss of motor nerve cells and their axons that no longer have connections with muscle (6). This atrophy progresses slowly over a period of months to years in adult mammals and results from trophic interdependence of motor neurons and their muscle targets for their mutual maintenance of normal metabolism and survival (5,6).

Myoelectric signals from more proximal existing musculature or portions of intact muscles that remain in partially amputated limbs can be used more readily for prosthetic guidance because of their higher signal amplitude (mV range) and accessibility. This use of different muscles as a source of information for prosthetic guidance requires retraining, since the muscles used are not concordant with the prosthetic function desired. Ideally, the neuromuscular signals obtained to guide a prosthetic device should be similar to those generated for muscles of the original limb for analogous functions. The use of muscle from portions of a donor muscle reinnervated by a lesioned nerve or fascicle of a nerve is one possible approach to obtain such information (1,7). However, the design and properties of an interface that could be used for this purpose have not been described. In this paper, we demonstrate the basic properties of such a biological interface between a fascicle of a lesioned nerve and a small strip of autologous donor muscle. Recording from such an interface may allow the acquisition of stable, naturally amplified signals from lesioned nerves. A preliminary description has been presented in abstract form (8).

METHODS

Twenty adult male Sprague Dawley rats (approximately 200 g) were utilized in all experiments under a protocol approved by the institutional animal care and use committee. The electrodes utilized for the isolation and recording of neuromuscular platform signals were of similar design to those used for chronic nerve recording and are illustrated in **Figure 1A** (3). Platinum iridium wire (100 μ, Thomas Scientific) was used for electrodes and initially for lead connections. Lead wires to the connector were later replaced with spiral wire leads encased in silicone tubing (Biopotential leads, Data Sciences International). The cuff consisted of a 4-mm silicone tube (O.D. 4 mm, I.D. 2 mm) with a single lengthwise slit to allow the electrode to be wrapped around an isolated muscle fascicle. The three electrode wires were constructed in two different designs, one in a discontinuous loop around the inside of the tube (**Figure 1A**) and the other as bare wire tips that protruded approximately 0.2 mm into the tube. Electrodes were spaced evenly within the tube at a distance approximately 1 mm apart. Lead wires were separated and encased in medical-grade silastic adhesive and attached to a connector also encased in silastic. The lead wires and connector were implanted under the skin for access at the time of evaluation. With the animal under Nembutal anesthesia (40 mg/kg), an incision was made on the lateral thigh over the palpable border of the femur. A slip of muscle approximately 1.5 mm in diameter was isolated from the gluteus muscle, which inserts on the proximal femur. The original origin and insertion of the muscle slip were maintained. Care was taken to ensure that the diameter of the slip was smaller than the diameter of the tube to avoid pressure ischemia. The slip was isolated close to the muscle's attachment to the femur, for stability. The silastic tube containing the electrodes was placed around the muscle slip, and the tube was sutured closed with two 7-0 sutures. A suture was placed on either end of the tube and passed through muscle attaching close to the femur, for stabilization. The adjacent sciatic nerve was then exposed by separating the muscle fascia. The peroneal nerve fascicle was dissected free and cut distally so that the proximal nerve stump could be mobilized and sutured into one end of the electrode tube over the muscle slip (**Figure 1B**).

After a period of 4 weeks, the animal was again anesthetized, the interface and the nerve graft were exposed, and recordings were made by stimulating the nerve fascicle and recording through the electrode leads. Recording instrumentation initially consisted of a Cadwell Sierra EMG/EP Model 6200A System (Cadwell Laboratories, Inc., Kennewick, WA) and, in later experiments, PowerLab 16s recording system (ADI Instruments, Mountain View, CA). The grafted nerve fascicle was stimulated initially with a 0.5-mA, 0.1-ms pulse, which was averaged over 10 stimulations. The amplitude of stimulation was then incremented in 0.5-mA steps until no change in the amplitude of the muscle action potential was obtained. In some instances, recordings were also made directly from the portion of the muscle slip within the tube with a tripolar needle electrode (Cadwell Laboratories, Inc., Kennewick, WA) to compare recorded electrode properties with unit activity

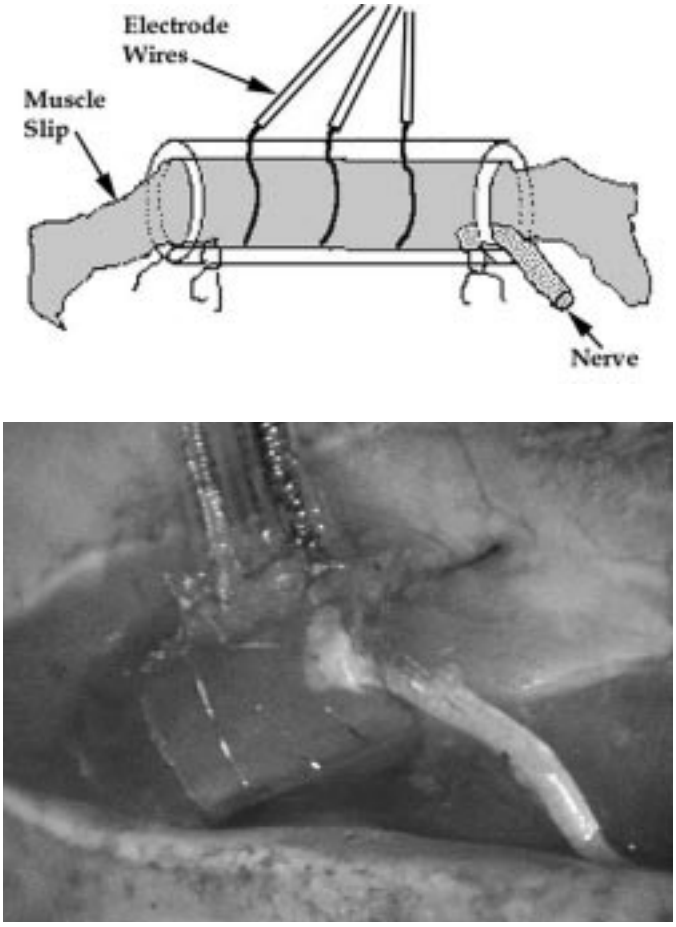

Figure 1.
A. Schematic of the electrode design with a muscle slip and grafted nerve. The tube is approximately 4 mm in length. Electrode contacts were either wire ends or circumferential 100-μ platinum wire. **B.** Micrograph of a device *in situ*.

detected with an independent electrode. The native muscle innervation was dissected out from the area of the sciatic notch and stimulated to examine possible interference with the signal. At the end of the recording session, the animal was killed with an overdose of anesthesia and the tube electrodes with their contents were collected for histological analysis. The electrodes were immersion fixed for 24 h in a fixative (2 percent glutaraldehyde, 2 percent paraformaldehyde, 0.1-M phosphate, pH 7.2); after which, the tube and electrodes were dissected free and fixation of the interface continued for 2 to 3 days. The interface was divided into proximal (nerve entry zone) and distal segments, postfixed in osmium tetroxide (2 percent in 0.1-M phosphate for 6 h), dehydrated, and embedded in plastic (Epon). Longitudinal sections of the proximal segment and cross sections of the distal segments (0.5μ) were collected on an MT-2 ultramicrotome and stained with toluidine blue.

RESULTS

Histology

Histological examination of the isolated slip of a host muscle typically showed a cord of intact muscle within the tube, surrounded by a layer of connective tissue next to the tube walls (**Figure 2A, B**). No appreciable degeneration of muscle myotubes was evident, although it may have occurred at an earlier time. In 18 of 20 successful interfaces examined, the implanted nerve was found to be well integrated into the muscle slip, inside the connective tissue sheath. Axons from the peroneal nerve fascicle could be seen on the surface of the central muscle core and integrating themselves and among the myotubular elements (**Figure 2C**, **Figure 2D**). The proportion of the cross section at the midpoint of the tube occupied by muscle fibers was approximately 2.0±0.6 mm^2 with an average thickness of connective tissue band of 160±110 (S.D.) μm. Histological examination of electrophysiological failures (see below) suggested that failures resulted from avulsion of the nerve fascicle from the tube or in one case, an infection process that had infiltrated along the connector leads into the interface.

Electrophysiological Assessments

Stimulation of the foreign nerve to the muscle slip in graded steps produced increasing compound muscle action potentials of varying amplitudes, but generally in the range of 0.5 to 2.0 mV (**Figure 3A**) with a latency to onset of approximately 2 ms. The average (±S.D.) maximal muscle action potential amplitudes and latencies to onset obtained upon supramaximal stimulation of the foreign and native nerves are shown in **Table 1**. Visible contractions of the muscle slip could be observed with stimulation of the foreign nerve in 18 of 20 cases. Stimulation of the native innervation to the gluteus muscle produced varying degrees of response (**Figure 3A**, bottom trace; **Table 1**). This suggested an incomplete disruption of the native innervation to the isolated muscle slip. Potential passive signal conduction from adjacent musculature was examined through direct stimulation of the gluteus muscle with an intensity sufficient to produce a contraction near the interface. This procedure did not produce a detectable signal from the interface electrode.

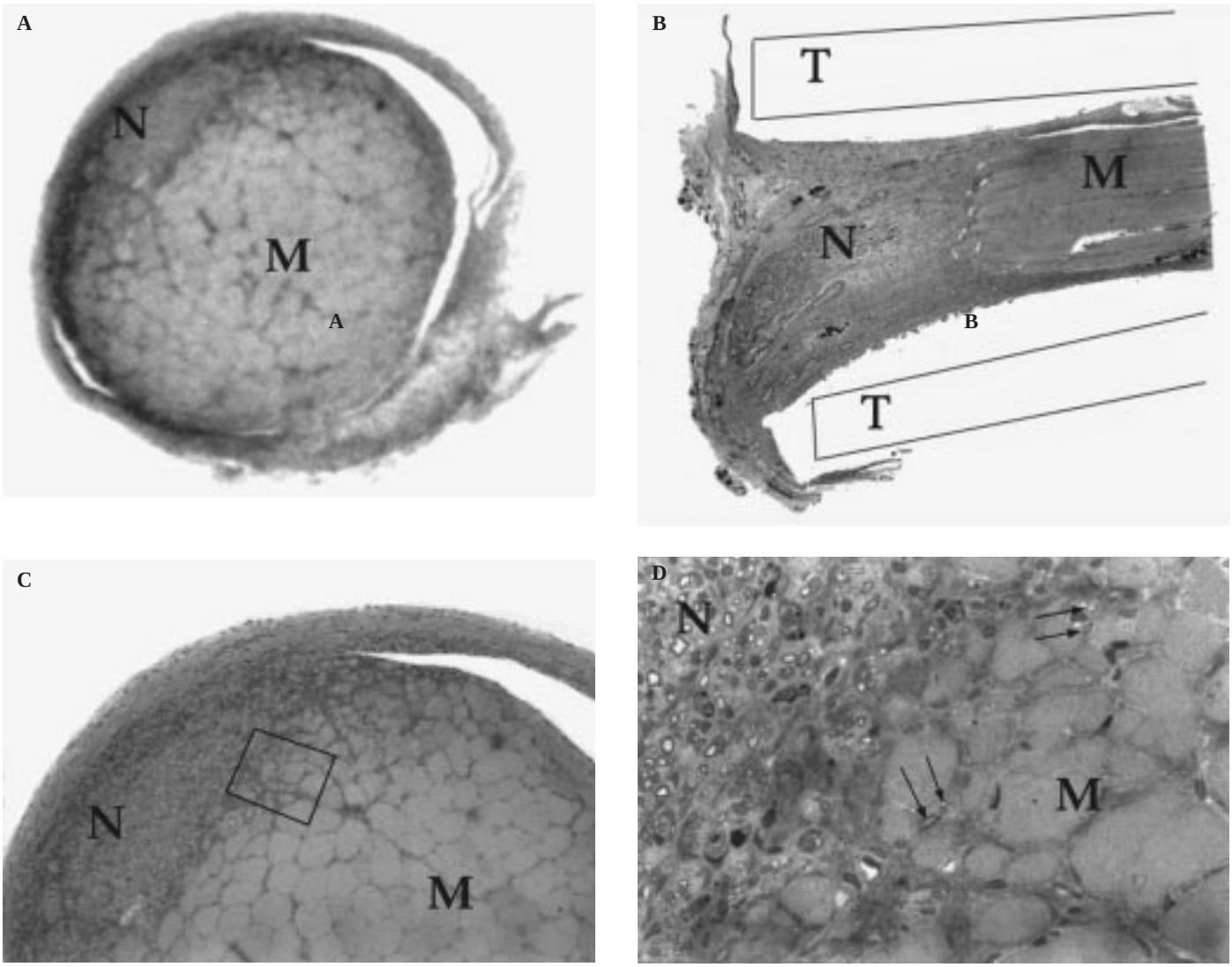

Figure 2.
Cross section of an interface of a muscle slip with a grafted nerve. **Top:** Low magnification views of the fascicle within a tube showing nerve (N) and muscle (M) segments in cross (**A**) and longitudinal (**B**) sections. The position of the tube (T) is shown in **B**. **Bottom: C** and **D**. Progressively higher magnification views of the nerve-muscle interface and axons within the muscle slip. The box outlined in **C** is shown in **D**. Axonal profiles (arrows) can be identified among the muscle fibers.

The configuration of the electrode within the tube yielded different signal complexities. Interface electrodes with wires that looped around the slip yielded muscle action potentials similar to those shown in **Figure 3A**. A tripolar needle electrode inserted in the muscle slip within the tube yielded more complex patterns, similar to unit activity (**Figure 3B**). Platform electrodes with only short, bare wire tips exposed to the fascicle also produced more complex response patterns similar to the tripolar needle electrode (**Figure 3B**, lower trace). However, a lower signal amplitude accompanied the increased signal complexity.

DISCUSSION

The data demonstrate that naturally amplified motor nerve signals can be obtained from lesioned nerves by allowing them to innervate isolated slips of host muscle in the environment of a recording electrode. The use of a tube as part of the electrode to surround the interface gave a reliable innervation of the muscle slip without appreciable outgrowth of the nerve into adjacent tissues. The tube electrode design also isolated the signal of the innervated slip from adjacent muscles in a manner similar to

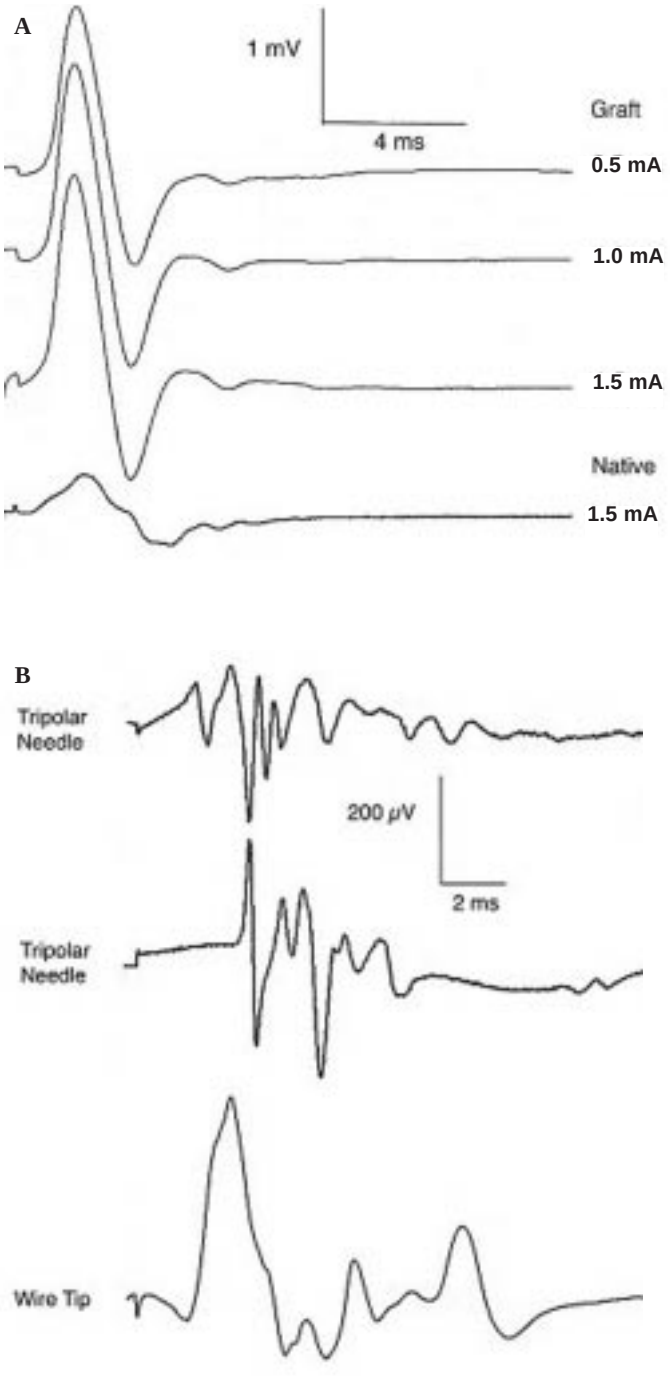

Figure 3.
A. The top three traces are signals recorded from muscle slips isolated in vivo from a loop electrode with increasing stimulation of the foreign nerve (0.5, 1.0, and 1.5 mA). The bottom trace shows the response from stimulation (1.5 mA) of the native innervation in the preparation used in **A**. **B.** The top two recordings were obtained from a tripolar needle electrode inserted directly into the muscle fascicle with stimulation of the foreign nerve. The bottom trace is a signal obtained from a wire point electrode upon stimulation of the foreign nerve.

Table 1.
Amplitudes and latencies of muscle action potentials.

	Amplitude (mV)	Latency to onset (ms)
Foreign nerve	1.0 ± 0.9	1.9 ± 1.1
Native nerve	0.65 ± 0.47	1.4 ± 0.6

nerve recording electrodes (3). The configuration of the electrodes in the tube clearly affects the complexity of the signal obtained under these conditions.

The responses that were obtained from the platform upon stimulation of the native innervation suggest a possible source of signal contamination from the host muscle. To some extent, the presence of this response appears to have reflected a conservative approach in our initial surgical implantation procedure, which was designed to ensure the survival of the muscle slip in the electrode. A more complete isolation of the muscle slip from the native muscle and aggressive physical and pharmacological denervation may produce more complete destruction of native innervation (9). Still, it is possible that native innervation could return over time to produce a cross talk between native and foreign muscle innervation in such a muscle mosaic system (10). This concern and the stability of the interface must be addressed with studies of longer duration.

From a functional standpoint, interfaces of this design could be used to obtain motor information from the separated fascicles of a lesioned nerve to operate a myoelectric prosthetic device (2). With the appropriate choice of nerve fascicles, interfaces could provide motor-control information for prosthetic functions, which are analogous to the information carried in the nerve. This should contribute to a greater ease in adaptation and use of the prosthesis. In addition to motor signals, sensory components of the foreign nerve may also innervate the platform and could possibly provide some sensory feedback information. This remains to be examined in the present model. With some design modification, such as an additional cuff electrode around the foreign nerve, it may also be possible to obtain electroneurograms from the nerve in addition to signals from the muscle slips and provide a mechanism to stimulate the nerve. From the electroneurogram, it is possible to filter sensory and motor component signals (4). This could also provide a means to distinguish electromyographic signals generated from the foreign nerve *versus* native innervation and add the ability to use signals from the nerve directly as part of the prosthetic control mechanism.

The successful reinnervation of muscle by the axons in the foreign nerve would be expected to attenuate the

degradation of signal amplitude observed in lesioned nerves with time after injury (5). This should be true for the proportion of axons of motor neurons in the nerve that reestablish trophic relationships as a result of connections. The reestablishment of neuromuscular synapses as part of the platform design suggest that the interface has the potential to be stable as a mechanism for prosthetic control. While the results of these experiments show the validity of a basic design for an interface, the practical application of the device as a signal source will require further characterization of its properties. In particular, it will be necessary to demonstrate that reliable motor signals can be obtained in freely moving animals and that these signals continue to convey the desired information over more extended periods of time.

CONCLUSION

Amplified motor signals can be obtained from lesioned nerves by allowing them to innervate isolated slips of host muscle in the *in vivo* environment of a recording electrode. This type of interface system may be useful in the extraction of information from and communication of information to lesioned nerves for use in the control of prosthetic devices. Further work is required to determine the long-term stability of the interface with respect to innervation by the foreign nerve, signal characteristics, and the fidelity of the signals to reflect the motor activity of muscles originally denervated.

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