Effects of Regional Stimulation Using a Miniature Stimulator Implanted in Feline Posterior Biceps Femoris

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Abstract—**The effects of placement of a miniature implantable stimulator on motor unit recruitment were examined in the posterior head of cat biceps femoris. The implantable stimulator (13-mm long × 2-mm diameter) was injected either proximally near the main nerve branch, or distally near the muscle insertion, through a 12-gauge hypodermic needle. Glycogen-depletion methods were used to map the distribution of fibers activated by electrical stimulation. Muscle fibers were found to be depleted at most or all proximodistal levels of the muscle, but the density of depleted fibers varied transversely according to the stimulus strength and proximity of the device to the nerve-entry site. Thus, muscle cross sections often had a "patchy" appearance produced because different proportions of depleted fibers intermingled with undepleted fibers in different parts of the cross section. In other preparations, the force of muscle contraction was measured when stimuli of varying strengths were delivered by the stimulator positioned at the same proximal or distal sites within the muscle. Devices placed close to the nerve-entry site produced the greatest forces. Those placed more distally produced less force. As stimulus current and/or pulse width increased, muscle force increased, often in steps, until a maximum was reached, which was usually limited by the compliance voltage of the device to less than the force produced by whole nerve stimulation.**

Index Terms—**Electrical stimulation, FES, FNS, paralysis, TES.**

I. Introduction

NEURAL prostheses to reanimate muscle use electrical stimulation to activate intact nerves that have lost their natural inputs as a result of disease or injury to the central nervous system. The electrical stimuli cause contractions by activating the most excitable elements of the neuromuscular complex, the preterminal axons or terminal arborizations of myelinated motor nerves. Repeated, chronic stimulation of motor nerves supplying a paralyzed muscle can increase muscle strength and aerobic capacity [1]–[3], and produce functionally useful movements (for review see [4]).

Several different approaches permit electrical stimulation of single muscles. These include the use of radio-frequency (RF) controlled, miniature single-channel stimulators that can be injected intramuscularly [5], [6], flexible wire electrodes that can be inserted percutaneously into muscles [7], [8], or surgically implanted, RF-controlled multichannel stimulators whose wire electrodes are attached either to the surface of the muscle (epimysial) [9] or around the muscle nerve (epineural) [10], [11].

Epineural, intramuscular, and epimuscular electrodes are all known to produce muscle contractions whose force can be graded by increasing the strength of stimulation pulses. However, when stimulating electrodes are placed directly on nerves, it can be difficult to grade muscle force in small increments because all of the alpha-motoneuron axons supplying different motor units have similar activation thresholds. Thus, small changes in stimulus strength can produce large shifts in motor-unit recruitment. Such shifts may occur even without changing the stimulus strength if the epineural electrodes move slightly with respect to the underlying axons in the nerve bundle. Embedded intramuscular electrodes are less sensitive to such problems because the greater intramuscular separation of motor nerve branches ensures a more gradual recruitment of motor axons when stimulus strength is increased. This advantage might have a "downside," however, when intramuscular devices are implanted in large muscles with specialized patterns of innervation and nonuniform motor-unit distribution. In such muscles, different parts of the muscle may be recruited nonuniformly. Such nonuniformities would introduce a significant level of complexity for a controller designed to produce a consistent level of muscle force for repeatable functional movements of a body part.

In the present study, we have explored the hypothesis that the intramuscular locus of muscle stimulation has a significant effect upon the distribution of active motor units and the strength of muscle contraction. Muscle stimulation was delivered using an implantable miniaturized stimulating device, chosen because of its fixed electrode geometry and ease of insertion into a particular subregion of muscle. Each miniature stimulator was inserted directly into the muscle mass through a large gauge hypodermic needle. Once in the muscle it was used to stimulate motor nerve branches with digitally controlled constant-current stimuli [5], [6]. The biceps femoris (BF) muscle was chosen for the present work because it is a large muscle whose motor-unit organization has previously been described in some detail [12], [13]. The previous studies showed that the muscle has three neuromuscular compartments, the posterior, middle, and anterior compartments, which are innervated by separate nerve branches and have different

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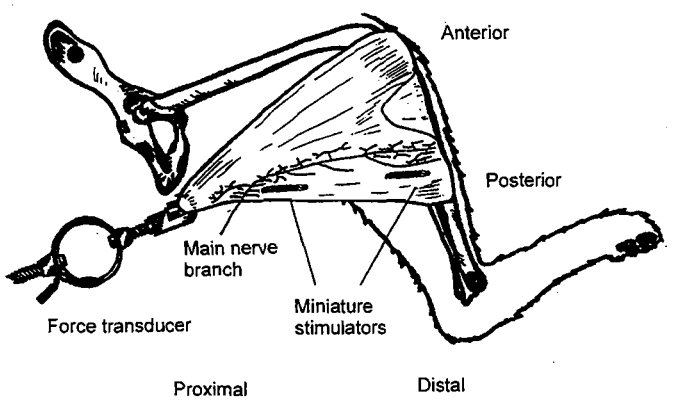

Fig. 1. Line drawing of the experimental preparation showing the location of the distal and proximal devices with respect to anatomical features of BFp. The neural branching pattern is adopted from Chanaud *et al.* (1991). The proximal end of the muscle is attached to a force transducer.

mechanical actions [12], [13]. The anterior and middle compartments lie in parallel without a distinct boundary to indicate their limits. The posterior compartment (BFp) is separated from the medial compartment at the proximal end by an internal aponeurosis originating at the posterior edge of the ischium. This aponeurosis serves as a site of insertion for fibers from the posterior part of the crural fascia. Muscle fascicles in all compartments are composed of muscle fibers only a few cm long which form overlapping arrays in order to span the distance between the origin and insertion of the muscle [12].

The distribution of activated fibers and the output force of recruited fibers were examined using two different methods. First, glycogen depletion [14] was used to assess the distribution of muscle fibers activated by devices in two different locations. Second, the forces developed by the BFp were measured in response to different levels of current delivery by microstimulators at these two locations. Thresholds to activate muscle fibers directly are higher than those to activate nerve; however, it may be possible for some muscle fibers next to the microstimulator to be stimulated directly. To test for this possibility, contractile force was measured again after administering a neuromuscular blocking agent.

II. Materials and Methods

A. Series 1

1) Glycogen Depletion of Motor Territories: Experiments were carried out on three cats (2.8–4.2 kg; either sex) anesthetized with sodium pentobarbital (initial dose, 35 mg/kg ip; supplemental doses, 5 mg/kg iv. to sustain deep anesthesia). Both BF muscles were exposed through posterior incisions above the popliteal fossa of each limb. A single microstimulator was injected into each muscle using a 12-gauge angiocath insertion tool (Becton Dickinson Vascular Access; Sandy, UT), under aseptic conditions. On one side of each animal the microstimulator was placed distally in posterior BF so that it lay parallel to the long axis of the distal muscle fascicles (Fig. 1). On the other side, it was placed proximally, next to the nerve-entry site. Each microstimulator was activated via an external coil (9-cm diameter × 1-cm height) placed over the implanted region to power and trigger the device at 40 pps for 300 ms every second, for a period of 1 h. Current strengths two or four times threshold for just-detectable muscle contraction were used. Animals were given a lethal injection of sodium pentobarbital and the right and left biceps muscles were removed.

2) Tissue Processing: Each of the muscles was weighed and cut into 11 to 12 blocks with dimensions of approximately 2 cm^3 as shown in Fig. 2. The blocks were mounted in a standardized orientation on perforated aluminum disks using embedding medium (OCT compound, Ames). They were coated with talcum powder and immersed into liquid nitrogen (−196 °C) for storage. The blocks were warmed to −20 °C and cut into 15- to 18-μm transverse sections. Two or more adjacent cryostat sections were retained at 2-mm intervals. Sections were placed on gelatin coated slides and dried in a 60 °C oven for 30 min. Tissue sections were reacted using the periodic acid-Shiff's (PAS) procedure for the demonstration of glycogen [15]. At least one additional section was taken from each block and stained for adenosine triphosphatase (ATPase) activity after formalin fixation and alkaline (pH 10.4) preincubation [16].

Stained muscle sections were examined under a light microscope to discriminate depleted fibers. These fibers were identified by blanched profiles indicating an absence of PAS reactivity. Fibers were classified as fast, glycolytic (FG), fast, oxidative-glycolytic (FOG) or slow oxidative (SO) by examining their staining profiles in adjacent sections reacted for ATPase activity, as described elsewhere [17]. A representative section from each level was magnified using a microfilm reader and its outline was traced. Regional variations in PAS staining were evaluated by inspecting each slide using light microscopy. The proportions of depleted and nondepleted fibers tend to change along fascicular borders, permitting each cross section to be divided into discrete regions whose outlines were recorded on the traced line drawings.

Territories containing depleted fibers were reconstructed from the various line drawings. For a single muscle section, regions containing different densities of depleted fibers were first identified and mapped as discrete zones on the line drawing of the muscle section. The fraction of the total cross-sectional area occupied by each zone was then calculated by digitizing the areas of the zones and the cross section as a whole, using the software package Bioscan Optima, Version 2.

Volume measurements were made for both the muscle as a whole and for the "depleted subvolume." Depleted subvolumes were defined as those regions containing greater than 10% depleted fibers. Volume calculations were made using the following formula:

$$V = \sum_{i=0}^{i=n} \frac{(A_i + A_{i+1})}{2} h_{i,i+1}$$

where A is the total cross-sectional area of the muscle at a particular level and h is the distance between adjacent areas normal to the plane of the section. In order to illustrate the relative amount and location of the glycogen depletion graphically, additional models of the muscle were made by

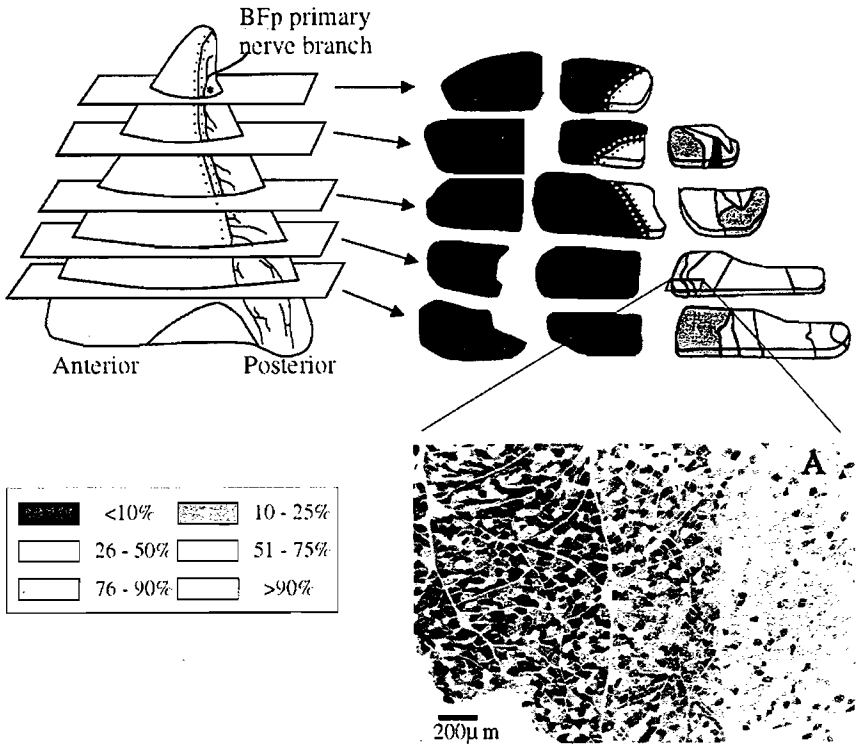

Fig. 2. Distribution of glycogen-depleted fibers following stimulation close to the proximal BF nerve branch at 2× threshold (asterisk shows location of the cathode). A representative section from each block is shown on the right, and the approximate location of the section within the whole muscle is shown on the left. The legend in the lower left indicates the proportions of depleted fibers in each section with black representing less that 10% depletion and white representing greater than 90% depletion. Below the right panel, a photomicrograph shows part of a cross section stained using the PAS method. Note the sharp borders between fascicles with different proportions of depleted fibers. Lightly stained fibers indicate glycogen depletion.

assuming the muscle cross sections to be elliptical. The major (a) and minor (b) axes of each ellipse was calculated from the cross-sectional areas using the relationship $a = 9b$, which formed an ellipse that best fit the actual muscle shape. The results of these calculations were used to reconstruct a three-dimensional (3-D) image using the software package MasterCAM.

Finally, the overall proportion of depleted fibers, expressed as "percent depletion," was estimated for each muscle. Depleted subvolumes were categorized into one of six depletion levels: <10%, 10%–25%, 26%–50%, 51%–75%, 76%–90%, and >90% depletion. The percent of muscle containing each depletion level was then determined. The overall percent depletion of the muscle was determined by multiplying the mid-value of each of the six depletion levels by the percent of the total muscle containing that level and summing these values for each of the six levels.

B. Series 2

1) Force Measurements: In three cats, the BF was exposed unilaterally through a posterior incision. The limb was stabilized by attaching bone screws to the tibia and fibula. The screws were secured to a frame. A small piece of bone at the ischial origin of BF was broken free from the pelvis and attached to a force transducer. The force transducer (linear calibration up to 35 N; compliance 8.9 μm/N) was attached to a motor-driven puller that was used to fix whole-muscle length. A microstimulator was placed in either the proximal or distal part of the posterior BF, and was used to elicit a contraction. All nerve branches except those entering the posterior compartment of the BF were cut. Animals were maintained at a normal body temperature of 37 °C throughout the procedure and intravenous saline was administered to maintain normal body fluid. The output force was graded by increasing the current level incrementally while maintaining the pulse width at either 100, 127, or 250 μs. A nerve cuff was placed around the sciatic nerve to produce contractions of the whole compartment, whose force was also measured. Forces produced by isometric twitches and trains (40 pps for 300 ms) were recorded and displayed on an oscilloscope. At the end of the experiment the animal was connected to a ventilator and intravenous gallamine triethiodide (5-mg/kg weight, Flaxedil 40, R.P. Pharma Inc., Montreal, PQ, Canada) was administered. Stimulation was repeated according to the same protocol described above, and the output forces were again measured. Animals were euthanized with a lethal injection of sodium pentobarbital.

III. Results

A. Glycogen Depletion

In all cats, stimulus pulses delivered by a single stimulator implanted either proximally next to the nerve-entry zone, or distally near the muscle insertion activated a muscular strip originating on the posterior side of the proximal tendinous band and extending to the lower crural fascia. The extent of

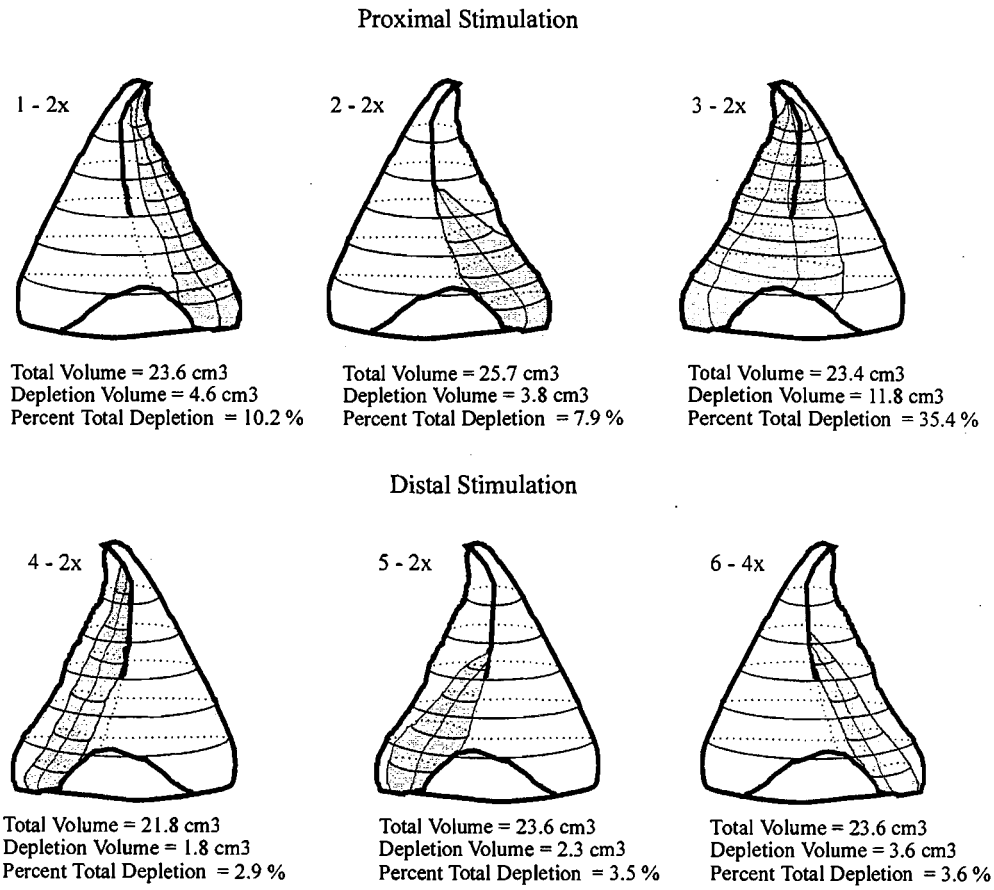

Fig. 3. Diagrammatic reconstruction to show depleted subvolumes in six muscles. The top three muscles were stimulated at 2× threshold current using a stimulator placed close to the nerve entry zone, whereas the bottom three muscles were stimulated at either 2× or 4× threshold current using a stimulator placed distally. Below each muscle are shown the measures of depletion volume and estimated percent depletion.

each territory and apparent strength of the contraction appeared to be related both to the location and the strength of the focal stimulus. Contractions elicited using a device near the nerve-entry zone were typically stronger and appeared to involve more of the muscle than those obtained when stimulated using a distally placed device.

Histochemical analysis showed that prolonged, intermittent stimulation altered the PAS reactivity of many muscle fibers throughout the region that had been observed to contract visibly. Transitions between regions containing differing percentages of depleted fibers were discrete rather than graded. A line could often be drawn between fascicles containing a predominance of depleted fibers and fascicles in which depleted fibers were present in much lower proportions (photomicrograph, Fig. 2). The mosaic of discrete zones containing different proportions of depleted fibers gave the muscle sections a "patchy" appearance. However, no other obvious cytological features generally distinguished the zones from one another. The zones were separated only by thin strands of perimysium, like those surrounding bundles of muscle fibers elsewhere. Similar zones of depleted fibers were found at all proximodistal levels of the muscle, from the distal fascia to the proximal tendinous band. This suggested that the zones were the cross-sectional representation of subvolumes extending proximodistally in parallel along the length of the muscle. In some muscles, the territory appeared to be confined to fiber fascicles with origins along the more distal part of the aponeurosis (shaded region in Fig. 3). In these cases, depleted fibers were not present, or were rare, in sections through the most proximal part of the muscle.

The volume of muscle in which depleted fibers constituted more that 10% of fibers in muscle-fiber fascicles ("depletion volume") was found to vary with placement and strength of the stimulus. When a stimulator was placed near the nerve-entry zone of the muscle, a larger and more thoroughly depleted subvolume was produced (Fig. 3). For example, a stimulator near the nerve entry region stimulated at 4× threshold produced a depletion volume of 11.75 cm^3 with a total percent depletion of 35%, whereas the stimulator placed distally and stimulated at 2× threshold produced a depletion volume of 1.75 cm^3 with a total percent depletion of only 3%.

B. Force Measurements

Forces produced by stimulating the muscle distally at all current strengths were much smaller than those generated by stimulating the muscle nerve supplying posterior biceps. Current strengths similar to those used in the glycogen-depletion studies produced twitch forces of 8% to 21% of maximum at 2× threshold current and 18% to 35% maximum at 4× threshold current depending on the site of distal placement. When a device was placed proximally in the muscle, close to

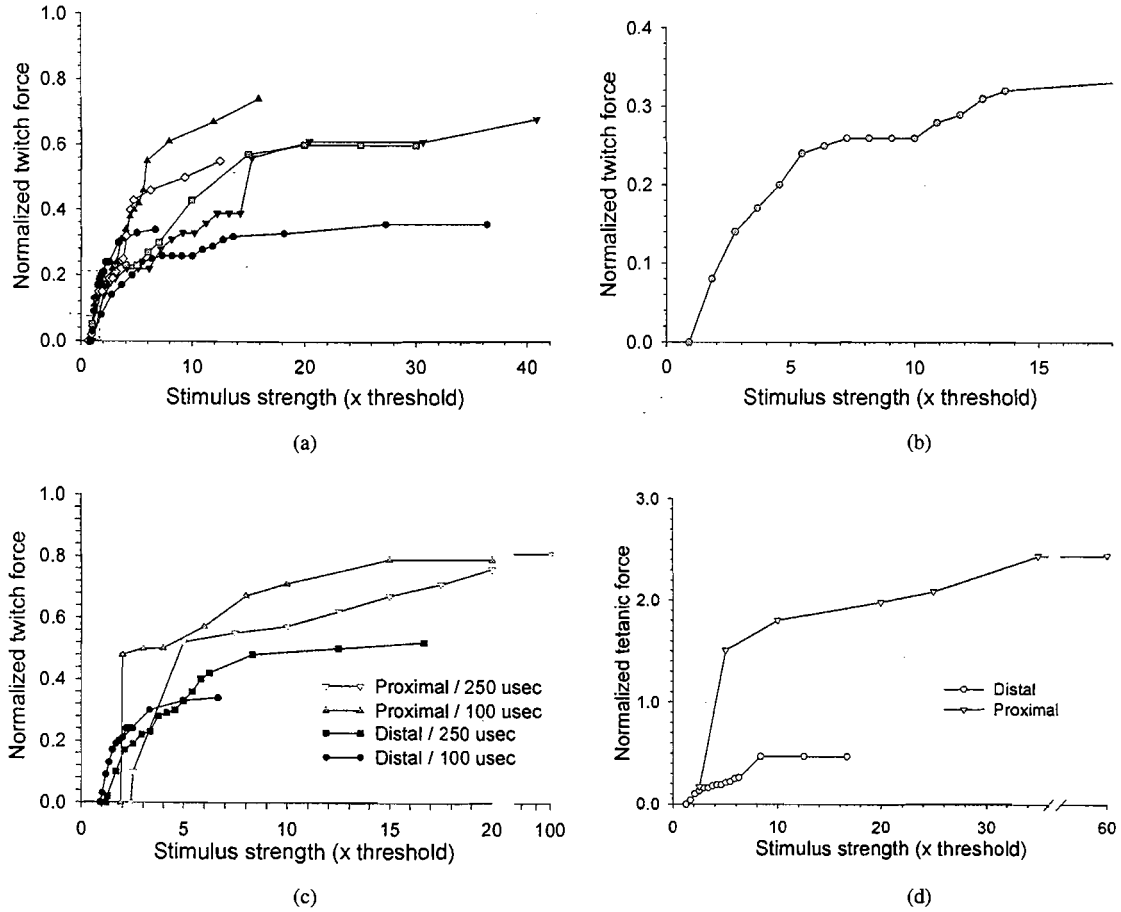

Fig. 4. Measured force output (normalized to maximum force) as a function of applied stimulus strength expressed as multiples of threshold. (a) All devices placed distally in the muscle and activated with a pulse width of 100 μs. (b) Multiple stages of force recruitment in a single muscle. (c)–(d) A comparison of the twitch and train forces generated by a device placed distally compared to one placed proximally.

the nerve-entry region, maximum twitch forces produced by these devices increased to 40%–80% of maximum (Fig. 4). Total recruitment of the posterior biceps could be produced when a single device placed next to the nerve-entry region was used to deliver current pulses 5× threshold current at 40 pps. Moreover, additional increases in current amplitude resulted in forces larger than those obtained by direct stimulation of the BFp nerve. This result occurred despite the fact that the nerve bundle to the adjacent compartment had been cut, presumably because the current spread occurred across the aponeurosis and through the muscle and was able to elicit contractions in nerve branches distal to the site of nerve section. One example of such a result is shown in Fig. 4(d), where a device placed proximally in the muscle and stimulated at 40 pps caused the muscle to generate a force of 151% of the maximum produced by posterior biceps when stimulated using a cuff on the sciatic nerve.

The contractions produced by a device placed distally in the muscle were not only less forceful but also showed lower slope of force versus stimulus strength (normalized to supramaximal) compared to those produced more proximally. Fig. 4(c) shows the forces produced when a device was placed either distally or proximally in the muscle. In all cases, gradual increases in pulse amplitude caused additional recruitment, typically as steps in which a relatively abrupt increase in force was followed by a plateau in force [Fig. 4(b)]. These steps were repeated until the amplitude of the pulses reached 16 mA, a value corresponding to the limit of current output dictated by the compliance voltage. Beyond this pulse amplitude, only increasing the pulse width to produce a larger charge per pulse could produce increases in force. Experiments repeated using large pulse widths of 250 μs demonstrated steeper rates of force recruitment with higher final maximum force levels [Fig. 4(c)].

Blockade of neuromuscular synaptic transmission by intravenous gallamine triethiodide resulted in a complete loss of visibly detectable contractions or measurable output force in response to electrical stimulation of the whole muscle nerve. Contractions were also abolished at most levels of stimulation using microstimulators. However, using pulse widths of 250 μs and maximum current levels of 16 mA, twitches were sometimes seen in a few muscle fibers immediately adjacent to the effective cathode of the stimulator.

IV. Discussion and Conclusions

In the present study, we analyzed the effects of focal electrical stimulation on the recruitment of motor units in posterior BF of the cat. Histochemical analysis and force measurements demonstrated that the position of the device was a critical factor that determined the capacity of the device to recruit

muscle fibers. With careful placement, however, a single stimulator was able to elicit contractions that were equally forceful to those produced using a nerve cuff. Focal stimulation at relatively low current strengths or at more distal sites most commonly produced nonuniform activation of muscle fibers as demonstrated by patchy patterns of glycogen-depletion.

A. Histochemical Assessment of Muscle-Fiber Activity

The distribution of active fibers depleted by focal stimulation was assessed using the glycogen-depletion method [14], in which the level of glycogen within a muscle fiber is employed as an index of its recent contractile history. This method is most reliable for muscles in which the majority of fibers have high glycolytic capacities and readily use their glycogen stores when driven to contract repetitively [14]. Fast-glycolytic (FG) fibers deplete most easily, after only a few minutes of stimulation, but slow-oxidative (SO) fibers have been reported to contain glycogen after as much as 1 h of stimulation [18], [19]. The cat posterior BF muscle appears ideal for study with the glycogen-depletion technique because it is composed almost exclusively by fast fiber subtypes (64% FG, 32% FOG, 4% SO fibers, [13]. However, our study confirmed observations by Smits *et al.* [20] and Thomson *et al.* [21] that at least some SO fibers can also be depleted using long regimes of muscle stimulation.

Glycogen-depletion of BFp resulted in cross sections that had a "patchy" appearance due to the uneven depletion of fibers. An uneven distribution of PAS-reactive fibers has been reported previously. For example, the glycogen-depletion patterns produced by stimulating rat tibialis anterior through an embedded pair of wire electrodes resulted in three distinct regions containing different proportions of depleted fibers [22]. Three-dimensional analysis of depleted regions in the present study suggested that the fascicles containing depleted fibers extended rostrocaudally to span the length of the muscle. This result agrees with an electromyogram study performed by Chanaud *et al.* [12], in which low-threshold stimulation of the BFp nerve resulted in the contraction of a band of muscle spanning the length of the muscle. Muscle fibers in BF are only 2–3 cm in length [12]. Thus, the present and previous observations suggest that motor axons must branch extensively to innervate fibers at different rostrocaudal levels of the fascicle.

At the proximal end of the muscle, all of the motor axons converge into a single bundle lying close to the stimulator. More distally, branches separate as they approach the muscle insertion. Thus, it might be expected that a pulse of similar stimulus strength would excite fewer of the more regionalized branches in the distal muscle. The nonuniform activation might be exacerbated if some motor axons were distributed asymmetrically in a proximodistal gradient, to supply more fibers at one muscle end, as has been described in anterior sartorius first by Thomson *et al.* [21] and later by Smits *et al.* [20]. However, the distribution of single motor units in BF has not yet been studied adequately to determine whether the patterns observed here can be ascribed to a nonuniform distribution of fibers comprising different motor units.

B. Force Measurements as an Index of Muscle-Fiber Recruitment

Physiological experiments further supported conclusions from glycogen-depletion studies that fibers could be recruited most efficiently by placing devices near the nerve entry zone at the proximal end of the muscle. Proximity to the motor nerve affected both the maximum force that could be evoked and the rate of development of that force [Fig. 4(b)]. A similar finding was reported previously by Grandjean and Mortimer [9] who examined the recruitment characteristics of muscle stimulated using mono- and bipolar epimysial electrodes attached to different muscle parts. They found that electrodes placed closest to the motor nerve could excite the muscle at the lowest stimulus strengths and could cause the graded force to increase at a faster rate. In the present study, single devices placed in the proximal muscle could sometimes be used to recruit the whole muscle. More often, however, the strength of the muscle contraction was found to plateau before maximal recruitment of the muscle was achieved. This result was attributed to limits in the compliance voltage of the stimulators used in this study. Although microstimulators were designed to deliver a stimulus pulse at an intensity of 30 mA, the compliance voltage of the presently available devices limited the usable current output in tissue to 16 mA [6].

The shape of the curve describing muscle force versus stimulus strength was distinctive and consistent, regardless of the position of the microstimulator within the muscle. These recruitment curves were seldom smooth, but instead exhibited a small series of "steps." Each consisted of a rapid increase of force that was followed by a flattening or plateau of the force [Fig. 4(a) and (b)]. These steps were imposed on an overall curve that was sigmoidal in shape. Popovic *et al.* [23] have also reported steps in the strength of muscle contractions when stimulating with intramuscular stainless-steel electrodes using pulse widths exceeding 100 μs.

The presence of steps in the recruitment curves suggests a discontinuous recruitment of motor units, whose forces must add in parallel. Recruitment of any single muscle unit will occur when the current field is large enough to evoke an action potential in any branch of the motor axon innervating its muscle fibers. Because of their different biophysical properties, large nerve axons that innervate large muscle units are activated by smaller stimulus pulses than small nerve axons [24]. This relationship of size to recruitment is opposite to that expected under normal physiological conditions of recruitment in which the smallest SO motor units are recruited first [25]. Various physiological studies have shown that FG muscle units have the largest numbers of muscle fibers and are innervated by the largest motor axons, whereas SO motor units have smaller motor axons and smaller numbers of muscle fibers [14], [18]. It was, therefore, not surprising that the recruitment curves presented in this study had a generally signmoidal shape, with a steeper slope at the lowest stimulus strengths and a flattening of the curve at higher stimulus strengths. However, this explanation is not sufficient to account for the appearance of smaller steps. They presumably arise because muscle-nerve bundles are distributed nonuniformly within the

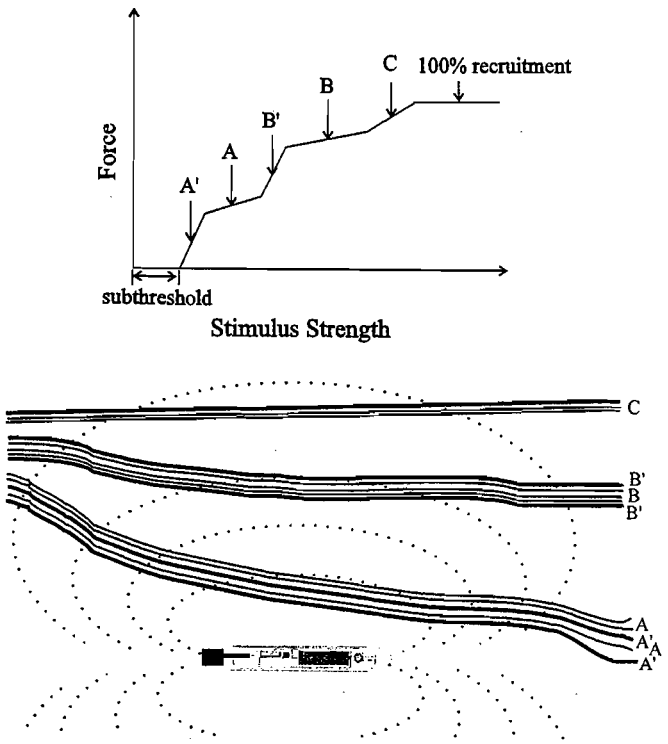

Fig. 5. Diagrammatic model of a sample recruitment curve that might result when stimulating a muscle containing multiple nerve branches. The first nerve fibers activated in the model are the largest fibers that lie closest to the device (A'), which presumably innervate fast-glycolytic (FG) muscle fibers. This produces a marked increase in force. Next, the remaining medium and small-diameter nerve fibers supplying fast-oxidative glycolytic (FOG) and slow-oxidative (SO) muscle fibers (A) are activated to produce a more gradual increase in force. This pattern is repeated as additional branches are recruited until 100% of possible recruitment is achieved.

muscle. As stimulus strength increases, it will first cause the rapid progressive recruitment of axons with relatively similar thresholds in the closest nerve bundle. When all of these axons are activated, a larger increase in stimulus strength might be needed before even the largest axons in a more distant bundle are activated (Fig. 5). The rate of recruitment of additional nerve branches will depend on the exact location of the electrode within the muscle. The number of steps in a particular recruitment curve may reflect the number of nerve branches that are activated progressively until force production plateaus with maximal stimulation. Note that axons in the more distant nerve branches that are branches of axons already recruited in closer nerve branches cannot contribute additional force. Thus, the size of successive steps might be expected to decrease.

It came as no surprise that the maximum force generated at a specified level of current delivery could be increased by an increase in the pulse width of the stimulus. There is a well-recognized inverse relationship between the stimulus strength and the pulse duration needed to bring an excitable tissue to threshold [26], because both of these factors affect charge. Increases in pulse width using a constant-current increases charge and thereby increases the number of motor units that can be stimulated to contract. This relationship proves important from a practical viewpoint because it can be used to extend the output range of compliance limited devices.

C. Neuromuscular Stimulation as a Clinical Tool

The relationship between recruitment and electrode position provides guidance for the clinical use and expected performance of FNS systems that use miniature implanted stimulators as their stimulus source. Any neuromuscular stimulator designed to be part of a neural prosthesis must produce consistent gradable contractions that are strong enough to elicit functional movements. The work presented here has shown that the electrical stimuli delivered by the implanted stimulator are strong enough to produce useful levels of contractile force, and that the magnitude of the force can be controlled by varying stimulus strength. However, both of these features are affected by device location. Results presented here suggest that devices placed close to a parent nerve branch will have lower thresholds compared to those placed distally. This might be a desirable characteristic because the power consumption of the device could be minimized by the lower current delivery. However, devices near a large nerve bundle may recruit all of the axons in the bundle with only modest increments in stimulus strength. In order to produce smoothly modulated rather than jerky movements, it may prove desirable to place the implanted stimulating device at some distance from the parent nerve bundle. In large or compartmentalized muscles, implantation of two or more well-spaced devices may be necessary to ensure the recruitment of fibers throughout the whole muscle. The modular design of the microstimulators employed in this study facilitates the addition of new channels as deemed necessary for the desired clinical function.

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REFERENCES

[1] I. Arvidsson, H. Arvidsson, E. Eriksson, and E. Jansson, "Prevention of quadriceps wasting after immobilization: An evaluation of the effect of electrical stimulation," *Orthopaedics*, vol. 9, p. 1519, 1986.

[2] K. T. Ragnarsson, "Physiologic effects of functional electrical stimulation-induced exercise in spinal cord-injured individuals," *Clin. Orthop., Rel. Res.*, vol. 233, pp. 53–63, 1988.

[3] R. M. Glaser, "Functional neuromuscular stimulation exercise conditioning of spinal cord injured patients," *Int. J. Sports Med.*, vol. 15, pp. 142–148, 1994.

[4] G. M. Yarkony, E. J. Roth, G. Cybulski, and R. J. Jaeger, "Neuromuscular stimulation in spinal cord injury I: Restoration of functional movement of the extremities," *Arch. Phys. Rehab.*, vol. 73, pp. 78–86, 1992.

[5] G. E. Loeb, C. J. Zamin, J. H. Schulman, and P. R. Troyk, "Injectable microstimulator for functional electrical stimulation," *Med. Biol. Eng., Comput.*, vol. 29, pp. 13–19, 1991.

[6] T. Cameron, G. E. Loeb, R. A. Peck, J. H. Schulman, P. Strojnik, and P. R. Troyk, "Micromodular implants to provide electrical stimulation of paralyzed muscles and limbs," submitted for publication.

[7] P. E. Crago, P. H. Peckham, J. T. Mortimer, and J. P. Van Der Meullin, "The choice of pulse duration for chronic electrical stimulation via surface, nerve, and intramuscular electrodes," *Ann. Biomed. Eng.*, vol. 2, pp. 252–264, 1974.

[8] P. H. Peckham, M. W. Keith, and A. A. Freehafer, "Restoration of functional control by electrical stimulation in the upper extremity of the quadriplegic patient," *J. Bone Joint Surg.*, vol. 70, pp. 144–148, 1988.

[9] P. A. Grandjean and J. T. Mortimer, "Recruitment properties of monopolar and bipolar epimysial electrodes," *Ann. Biomed. Eng.*, vol. 14, pp. 53–66, 1986.

[10] P. H. Gorman and J. T. Mortimer, "The effect of stimulus parameters on the recruitment characteristics of direct nerve stimulation," *IEEE Trans. Biomed. Eng.*, vol. BME-30, pp. 407–414, 1983.
[11] H. Thoma, W. Girsch, J. Holle, and W. Mayr, "Technology and long-term application of an epineural electrode," *Trans. Amer. Soc. Artif. Intern. Organs*, vol. 35, pp. 490–494, 1989.
[12] C. M. Chanaud, C. A. Pratt, and G. E. Loeb, "Functionally complex muscles of the cat hindlimb II. Mechanical and architectural heterogeneity within the biceps femoris," *Exp. Brain Res.*, vol. 8, pp. 257–270, 1991A.
[13] ——, "Functionally complex muscles of the cat hindlimb V. The roles of histochemical fiber-type recanalization and mechanical heterogeneity in differential muscle activation," *Exp. Brain Res.*, vol. 85, pp. 300–313, 1991B.
[14] R. E. Burke, D. N. Levine, P. Tsairis, and F. E. Zajac, "Physiological types and histochemical profiles in motor units of the cat gastrocnemius," *J. Physiol.*, London, vol. 234, pp. 723–748, 1973.
[15] R. A. B. Drury and E. A. Wallington, *Carleton's Histological Technique*. Oxford, U.K.: Oxford Univ. Press, 1980.
[16] L. Guth and F. J. Samaha, "Qualitative differences between actomyosin ATPase of slow and fast mammalian muscle," *Exp. Neurol.*, vol. 25, pp. 138–152, 1969.
[17] J. B. Peter, R. J. Barnard, V. R. Edgerton, G. A. Gillespie, and K. E. Stempel, "Metabolic profiles of three fiber types of skeletal muscle in guinea pigs and rabbits," *Biochem.*, vol. 11, pp. 2627–2633, 1972.
[18] R. E. Burke, D. N. Levine, M. Salcman, and P. Tsairis, "Motor units in cat soleus muscle: Physiological, histochemical and morphological characteristics," *J. Physiol.*, London, vol. 238, pp. 503–514, 1974.
[19] J. Toop, R. E. Burke, R. P. Dum, M. J. O'Donovan, and C. B. Smith, "2-Deoxyglucose autoradiography of single motor units: Labeling of individual acutely active muscle fibers," *J. Neurosci. Meth.*, vol. 5, pp. 283–289, 1982.
[20] E. Smits, P. K. Rose, T. Gordon, and F. J. R. Richmond, "Organization of single motor units in feline sartorius," *J. Neurophysiol.*, vol. 72, pp. 1885–1896, 1994.
[21] D. B. Thomson, S. H. Scott, and F. J. R. Richmond, "Neuromuscular organization of feline anterior sartorius: I. Asymmetric distribution of motor units," *J. Morphol.*, vol. 21, pp. 147–162, 1991.
[22] J. T. Mortimer and P. H. Peckham, "Intramuscular electrical stimulation," in *Neural Organization and Its Relevance to Prosthetics*, W. S. Fields and L. A. Leavitt Eds. Miami, FL: Symposia Specialists, 1973, p. 131.
[23] D. Popovic, T. Gordan, V. F. Fafuse, and A. Prochazka, "Properties of implanted electrodes for functional electrical stimulation," *Ann. Biomed. Eng.*, vol. 19, pp. 303–316, 1991.
[24] J. B. Ranck, "Which elements are excited in electrical stimulation of mammalian central nervous system: A review," *Brain Res.*, vol. 98, pp. 417–440, 1975.
[25] E. Henneman, "Functional organization of motoneuron pools: The size principle," in *Proc. Int. Union Physiol. Sci.*, 1977, vol. 12, p. 50.
[26] J. Erlanger and H. S. Gasser, *Electrical Signs of Nervous Activity*. Philadelphia, PA, Univ. of Pennsylvania Press, 1937.

Tracy Cameron (S'93-M'96), for a photograph and biography, see this issue, p. 1034.

Frances J. R. Richmond, for a photograph and biography, see this issue, p. 1035.

Gerald E. Loeb, for a biography, see this issue, p. 1035.