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Wide-pulse-width, high-frequency neuromuscular stimulation: implications for functional electrical stimulation

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Baldwin, Evan R. L., Piotr M. Klakowicz, and David F. Collins. Wide-pulse-width, high-frequency neuromuscular stimulation: implications for functional electrical stimulation. *J Appl Physiol* 101: 228–240, 2006. First published April 20, 2006; doi:10.1152/jappphysiol.00871.2005.—Electrical stimulation (1-ms pulses, 100 Hz) produces more torque than expected from motor axon activation (extra contractions). This experiment investigates the most effective method of delivering this stimulation for neuromuscular electrical stimulation. Surface stimulation (1-ms pulses; 20 Hz for 2 s, 100 Hz for 2 s, 20 Hz for 3 s) was delivered to triceps surae and wrist flexors (muscle stimulation) and to median and tibial nerves (nerve stimulation) at two intensities. Contractions were evaluated for amplitude, consistency, and stability. Surface electromyograph was collected to assess how H-reflexes and M-waves contribute. In the triceps surae, muscle stimulation produced the largest absolute contractions (23% maximal voluntary contraction), evoked the largest extra contractions as torque increased by 412% after the 100-Hz stimulation, and was more consistent and stable compared with tibial nerve stimulation. Absolute and extra contraction amplitude, consistency, and stability of evoked wrist flexor torques were similar between stimulation types: torques reached 11% maximal voluntary contraction, and extra contractions increased torque by 161%. Extra contractions were 10 times larger in plantar flexors compared with wrist flexors with muscle stimulation but were similar with nerve stimulation. For triceps surae, H reflexes were 3.4 times larger than M waves during nerve stimulation, yet M waves were 15 times larger than H reflexes during muscle stimulation. M waves in the wrist flexors were larger than H reflexes during nerve (8.5 times) and muscle (18.5 times) stimulation. This is an initial step toward utilizing extra contractions for neuromuscular electrical stimulation and the first to demonstrate their presence in the wrist flexors.

human; triceps surae; wrist flexors; isometric contractions; electromyography

NEUROMUSCULAR ELECTRICAL STIMULATION (NMES) is commonly used to restore or maintain motor function for people with movement disorders. NMES is typically delivered with large electrodes placed on the skin above the muscle belly, and contractions are evoked by activating the terminal branches of motor axons (3, 28). NMES normally involves frequencies between 20 and 50 Hz and pulse widths between 200 and 400 μ s (7) and should recruit motor axons preferentially to sensory axons (36, 37, 46). Thus traditional NMES is more conducive to direct activation of motor axons and less likely to evoke contractions through reflex pathways by stimulating sensory afferents. The electrical activation of motor axons recruits motor units in a disorderly manner, with a tendency toward a reversal of voluntary motor unit recruitment order; thus large-

diameter motor axons innervating highly fatigable fast-twitch muscle fibers are recruited first (39, 44). One problem for NMES is contractions evoked in this manner fatigue rapidly, and substantial recruitment of slow-twitch muscle fibers occurs only at higher stimulation intensities.

A potential solution to the fatigue associated with NMES is to evoke muscle contractions by activating motoneurons through reflex pathways. Similar to voluntary recruitment, motor units recruited via spinal pathways proceed in an order from smallest to largest diameter (20). Contractions should be more fatigue resistant than those evoked by direct motor axon activation, as the smallest diameter motor axons innervate the most fatigue-resistant muscle fibers (20, 31). Reflexive muscle activation with electrical stimulation can be achieved by optimizing the stimulation parameters to recruit sensory afferents using pulse widths between 0.5 and 1 ms (36, 37, 46). A unique feature of contractions evoked reflexively through afferent pathways is that torque climbs more than expected from motor axon stimulation as the frequency is increased and remains elevated when the stimulation frequency is reduced. Contractions evoked in this manner, using wide pulse widths (1 ms) and high frequencies (100 Hz), can produce up to five times more torque than expected from direct activation of motor axons alone (10, 11). These “extra” contractions depend on afferent input to spinal neurons as they are abolished during anesthetic nerve block proximal to the stimulation site (10, 11). Further evidence of spinal involvement includes the presence of extra contractions at stimulation intensities below motor threshold (11), residual electromyographic (EMG) activity beyond the stimulation period (10, 11, 33), and enhanced Hoffman (H) reflexes during stimulation capable of producing sustained EMG (50 Hz; Ref. 34) and maintaining extra contractions (20 Hz; Ref. 27). The presence of H reflexes during high-frequency stimulation supports the idea of reduced muscle fatigue during NMES as fatigue-resistant motor units dominate the soleus H reflex (8). An electrically induced physiological recruitment order via spinal reflex pathways may be beneficial for NMES applications where prolonged contractions are required for functional tasks (10). Additionally, the recruitment of slow-twitch muscle fibers may be useful in recruiting portions of paralyzed muscle not recruited by direct motor axon excitation to counter muscle atrophy (10) and the transition from slow- to fast-twitch muscle fibers.

The purpose of this study was to determine the optimal technique to evoke sustained contractions enhanced through

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spinal pathways (extra contractions) during NMES. Studies using high frequencies and wide pulse widths have stimulated directly over the muscle (10, 11, 33) or over the nerve trunk proximal to the muscle (26, 27, 34), and have focused exclusively on muscles of the lower leg. Thus the following two questions were raised: Are extra contractions evoked best by stimulating over the muscle directly or by stimulating the nerve trunk proximal to the muscle, and are extra contractions present in muscles other than those of lower leg? We hypothesized that no difference would exist between extra contractions evoked by either stimulation directly over the muscle or proximal to the muscle over the nerve and that extra contractions would be present in upper limb muscles such as the wrist flexors. In the upper limb, however, we expected extra contractions of lesser magnitude than in the lower limb as greater levels cortically induced presynaptic inhibition (PSI) are known to regulate upper limb muscles (2). The present experiments tested the above hypotheses by electrically evoking contractions in the plantar flexors and the wrist flexors. Electrical stimulation was delivered over the nerve proximal to the muscle or directly over the muscle at two intensities. The extent that extra contractions were present during the stimulation was evaluated and compared between stimulation types (nerve or muscle), between intensities, and between the upper and lower limbs. The consistency between consecutive contractions and the stability of each contraction was assessed because they are important for NMES. Portions of these experiments have been presented previously as an abstract (4).

METHODS

Subjects

These experiments were designed to evaluate the optimal delivery of electrical stimulation to evoke extra contractions that are consistent and stable in the ankle plantar flexors and wrist flexors. Stimulation was delivered over the nerve (nerve stimulation) proximal to the muscle and over the muscle belly (muscle stimulation). Experiments were conducted on the lower limbs of 10 subjects (8 men, 2 women; age range, 20–41 yr) and the upper limbs of 10 subjects (9 men, 1 woman; age range, 22–41 yr). Five subjects participated in both experiments, making the total number of subjects 15. Subjects were free from neurological and musculoskeletal disorders and participated after providing informed, written consent. Each experiment lasted ~2 h. Experimental protocol was approved by the University of Alberta Human Research Ethics Board and were conducted in accordance with the Declaration of Helsinki.

Protocol

Stimulation over the muscle belly is defined as muscle stimulation; however, this type of stimulation recruits muscle fibers via their terminal motor axon branches. Stimulation proximal to the muscle, over the nerve trunk, is defined as nerve stimulation. Maximal ankle plantar flexion or wrist flexion torque was measured during a 3- to 5-s maximal voluntary contraction (MVC) at the beginning of each experiment. Load cell measurements were sampled at 2,000 Hz.

Ankle plantar flexors. Subjects were seated comfortably with the right hip and knee flexed between 90° and 110° and the right foot fixed at 90° to a stationary footplate with straps to hold the foot and knee securely in place (Fig. 1A). The footplate transferred plantar

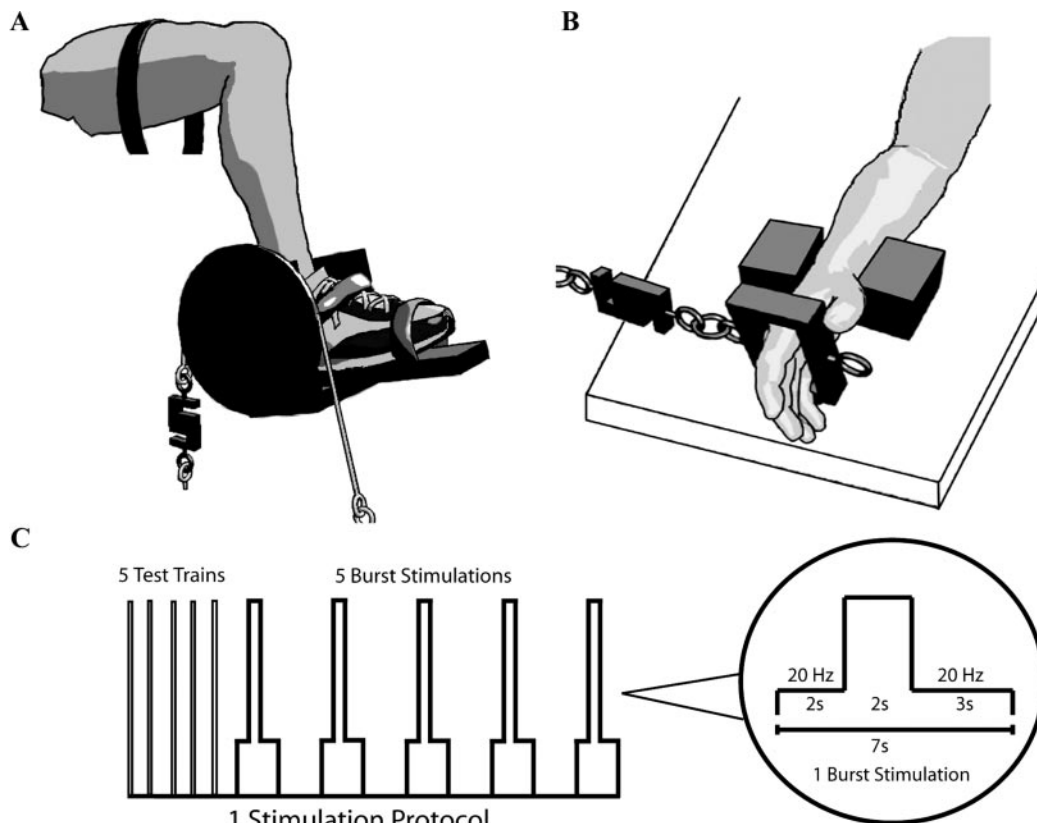


Fig. 1. Schematic diagram of the experimental apparatus used for the lower limb (A) and the upper limb (B). Torque was measured with a strain gauge, and each limb was fixed to ensure isometric contractions. C: schematic of stimulation protocol during a single trial. Individual test trains were separated by 5 s, and individual burst stimulations were separated by 10 s. A single-burst pattern is depicted in the balloon above the last burst stimulation.

flexion force about a 72-tooth cog wheel (22-cm diameter) attached to an S-type load cell (LCCB-500, Omega, Stamford, CT) to measure torque. Muscle stimulation electrodes were placed over the triceps surae. The proximal anode (15 × 3.5 cm) was placed midway across the gastrocnemius, ~12 cm distal to the crease of the popliteal fossa. The distal cathode (8 × 3.5 cm) was placed over the soleus below the gastrocnemius, ~15 cm distal from the center of the proximal electrode. Nerve stimulation electrodes were situated on either side of the crease of the popliteal fossa over the tibial nerve with an interelectrode distance of 1 cm. EMG recording electrodes were placed 1 cm apart over the distal aspect of the soleus, proximal to the Achilles tendon.

Wrist flexors. The subject's right arm rested on a table with the right hand secured in a neutral position (Fig. 1B). Padded blocks were fixed on either side of the wrist to reduce movement of the forearm. The hand apparatus was connected in series with an S-type load cell (SSM100, Interface, Scottsdale, AZ) to measure wrist flexion torque. A taut metal chain attached to the load cell restricted movement during the contractions. Muscle stimulation electrodes were placed over the wrist flexors. The proximal anode (5 × 3.5 cm) and distal cathode (4 × 3.5 cm) were placed 5 and 12 cm, respectively, distal to the crease of the cubital fossa with an interelectrode distance of 7 cm. Nerve stimulation electrodes (2.25 cm²) were placed proximal to the medial epicondyle on the medial-distal aspect of the humerus over median nerve with an interelectrode distance of 1 cm. EMG recording electrodes were placed as close to the flexor carpi radialis muscle as possible given the location of the stimulating electrodes, with an interelectrode distance of 1 cm. Anatomical differences between subjects warranted small variations in stimulating and recording electrode placement on both limbs.

Stimulation

Muscle stimulation was delivered using flexible electrodes (Electrosurgical Patient Plate 1180: Split, 3M Health Care, St. Paul, MN) cut to size. Nerve stimulation was delivered using Ag-AgCl surface electrodes (Vermed Medical, Bellows Falls, VT).

One-millisecond rectangular pulses were delivered using a Grass S88 stimulator connected in series with a Grass SIU5 isolator and a Grass CCU1 constant-current unit (Grass Instruments, AstroMed, West Warwick, RI), and stimulation current was measured (mA-2000 Noncontact Milliammeter, Bell Technologies, Orlando, FL). Stimulation intensity was adjusted based on the peak torque generated during test trains of five pulses at 100 Hz. Test trains were delivered at two intensities to evoke peak torques of 2 (low intensity) and 4% (moderate intensity) of the prerecorded MVC value. M-wave-H-reflex recruitment curves were created from responses to 40 stimuli delivered to the tibial and median nerves at intensities ranging from subthreshold for any response up to those two times the threshold for a maximal motor response (M_{max}). From the recruitment curves, maximal H reflex (H_{max})-to- M_{max} ratios were calculated.

The stimulation protocol is illustrated in Fig. 1C and consisted of two stimulation patterns; five test trains delivered 5 s apart; and five burst stimulations 10 s apart consisting of 20 Hz for 2 s, 100 Hz for 2 s, and 20 Hz for 3 s (adapted from Refs. 10, 11, 26). The burst pattern was chosen because it allows for a comparison of torque generated during the first 2 s of stimulation, where torque is produced primarily through the activation of motor axons, and the last 3 s of stimulation, where torque is the product of both peripheral and spinal contributions (10). This protocol was followed for nerve and muscle stimulation at low and moderate intensities. Subjects were instructed to remain relaxed and were encouraged to read during the experiments to divert their attention from the stimulation.

EMG

EMG was recorded using self-adhesive Ag-AgCl surface electrodes (2.25 cm² Vermed Medical, Bellows Falls, VT). EMG record-

ings (Octopus AMT-8, Bortec Biomedical, Calgary, AB, Canada) were preamplified with a gain of 500, band-pass filtered (30–1,000 Hz), and sampled at 2,000 Hz using a 12-bit National Instruments analog-to-digital converter (Austin, TX) connected to a computer running custom-written Labview software (National Instruments).

Data Analysis

For statistical analysis, data were averaged over 400-ms windows centered around 1 and 6 s into the stimulation and expressed as %MVC. Four aspects of the torque profiles considered to be important for NMES were quantified. 1) Absolute amplitude of the contraction produced was determined by the torque produced at 6 s into the stimulation. 2) Extra contraction amplitude, meant to represent the torque generated solely from spinal mechanisms, was assessed by the difference in torque after the 100-Hz stimulation (at 6 s) compared with before (at 1 s). 3) Consistency between successive contractions was measured by calculating the coefficient of variation (CV) between the torques produced during five consecutive burst stimulations at 6 s into the stimulation. 4) Stability within a contraction was calculated as the CV for each contraction over the last 2 s of each stimulation train. Torque data were resampled post hoc at 100 Hz for analysis.

M waves and H reflexes were quantified to explore the mechanisms underlying torque produced during nerve and muscle stimulation. EMG was analyzed only in subjects where M waves could be clearly identified during both types of stimulation. In most cases, the stimulus artifact during muscle stimulation prevented a clear measurement of the M wave; however, it was possible to record both waveforms from soleus for four subjects and the wrist flexors for three subjects at the low stimulation intensity. Responses were measured (peak to peak) during the 20-Hz segments of the burst stimulation and normalized to M_{max} . The single largest M-wave response from the recruitment curve was taken as M_{max} .

Statistics

Statistics were performed using Statistica software (StatSoft, Tulsa, OK). Paired *t*-tests were used on individual and group data to detect differences in absolute torques produced by each stimulation type and to detect significant differences in relative torques (extra contractions) within each stimulation type. Extra contractions were defined as a statistically significant increase in torque from 1 s into the initial 20-Hz stimulation period compared with 1 s into the 20-Hz stimulation following the 100-Hz "burst." Two-factor repeated-measures ANOVAs were used on group data to determine the influence of stimulation type (nerve and muscle stimulation) and intensity (low and moderate intensity) on the size of the extra contractions, using difference values calculated by subtracting the torque produced at 1 s from 6 s into the stimulation; on the consistency between contractions and the stability within a contraction, using the CV values (described above); and to compare the size of extra contractions between each muscle group (plantar vs. wrist flexors), using the difference values, generated by nerve and muscle stimulation at low and moderate intensities. Significant main effects and interactions were tested post hoc using Tukey's honestly significant difference test. Descriptive statistics are expressed as means (SD), and error bars in the figures represent 95% confidence intervals. An α level of 0.05 was used to evaluate statistical significance.

RESULTS

Electrical stimulation was delivered over the plantar and wrist flexors with parameters known to induce contractions through direct motor axon stimulation and excitation of spinal neurons through stimulation of primary afferents. Absolute and extra contraction amplitudes, along with the consistency between successive contractions, and stability within a single contraction were compared between nerve and muscle stimu-

lation at two intensities. Extra contractions were produced in the plantar and wrist flexors with nerve and muscle stimulation at low and moderate intensities. Moderate-intensity muscle stimulation of triceps surae produced the largest absolute torques, and low-intensity muscle stimulation evoked the largest extra contractions. Low-intensity tibial nerve stimulation produced the least consistent and stable contractions. Contraction amplitudes were similar for all conditions in the wrist flexors.

Contraction Amplitude

Plantar flexors. Torque profiles generated during five successive contractions during nerve and muscle stimulation are shown for a single subject in Fig. 2. Average torque profiles during the five test trains preceding the burst stimulations are also shown. Stimulus intensity was adjusted to evoke peak torques of 2% (low intensity) or 4% (moderate intensity) MVC during the test trains. Significant extra contractions were observed during all four types of stimulation. Torque between initial and subsequent 20-Hz stimulation periods increased from 1 to 3% MVC and 3 to 17% MVC during nerve (Fig. 2A) and muscle (Fig. 2B) stimulation, respectively, at a low stimulation intensity; and 4 to 12% MVC and 12 to 26% MVC during nerve (Fig. 2C) and muscle (Fig. 2D) stimulation, respectively, at a moderate stimulation intensity. Qualitatively, there were distinct differences between the torque profiles generated with nerve and muscle stimulation. For example, at the beginning of the stimulation, a large initial peak in the torque was observed during nerve stimulation (Fig. 2A), yet with muscle stimulation this peak was absent (Fig. 2B).

Group data displaying the results of stimulating the ankle plantar flexors are presented in Fig. 3. Similar to the single-

subject data in Fig. 2, a sharp increase in torque appears at the beginning of tibial nerve stimulation; however, a much smoother increase in torque occurs when muscle stimulation commences. Comparisons used for statistical analysis between initial and subsequent 20-Hz stimulation periods are displayed in Fig. 3B. Muscle stimulation at low and moderate intensities produced significantly larger absolute torques, 13.6 (SD 6.2) and 23.3 (SD 11.7) %MVC, respectively, during subsequent 20-Hz stimulation periods compared with nerve stimulation at comparable low [1.5 (SD 1.2) %MVC] and moderate [5.3 (SD 4.5) %MVC] intensities. Torques generated before the 100-Hz stimulation train (at 1 s) were significantly different between low-intensity nerve [1 (SD 0.4) %MVC] and muscle [3 (SD 1) %MVC] stimulation, and between moderate-intensity nerve [3 (SD 2) %MVC] and muscle [9 (SD 4) %MVC] stimulation. However, torques were similar during initial 20 Hz stimulation periods between moderate-intensity nerve stimulation [2.7 (2.4) % MVC] and low-intensity muscle stimulation [2.8 (SD 1.2) %MVC]. After the 100-Hz train (at 6 s), significantly ($P = 0.004$) greater torques were produced with low-intensity muscle stimulation [13.6 (SD 6.2) %MVC] compared with moderate-intensity nerve stimulation [5.3 (SD 4.5) %MVC]. Nerve stimulation at low intensity produced significant extra contractions in 3 of 10 individuals, and for the group ($n = 10$) torque increased significantly from 0.6 (SD 0.4) to 1.5 (SD 1.2) %MVC. Muscle stimulation at the low intensity evoked significant extra contractions in all subjects where torque increased significantly from 2.8 (SD 1.2) to 13.6 (SD 6.2) %MVC. Moderate-intensity nerve stimulation caused significant extra contractions in 8 of 10 individuals and significantly increased torque from 2.7 (SD 2.4) to 5.3 (SD 4.5) %MVC for the group. Moderate-intensity muscle stimulation produced

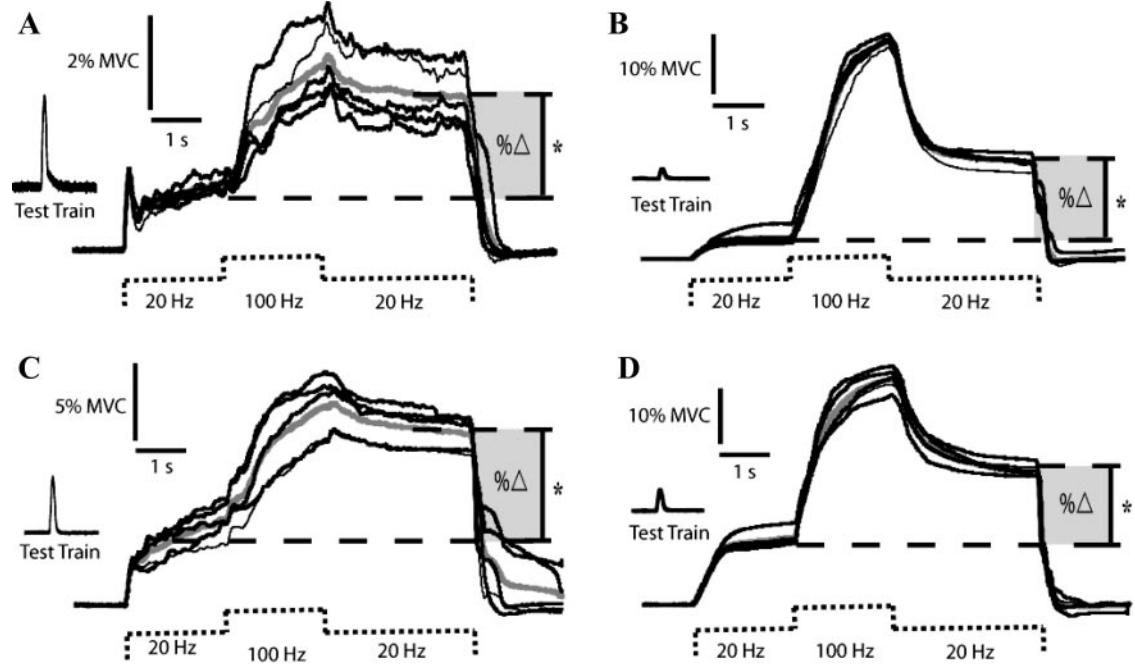


Fig. 2. Torque recorded from a single subject during tibial nerve and triceps surae stimulation at low (A and B) and moderate (C and D) stimulation intensities. Gray traces denote the mean of the 5 torque profiles (black traces). Gray regions between dashed lines represent the amount torque increased after, compared with before, the 100-Hz stimulation period (%Δ). MVC, maximal voluntary contraction. *Significant torque increases: 205%Δ, $P = 0.002$ (A); 397%Δ, $P < 0.001$ (B); 175%Δ $P < 0.001$ (C); and 126%Δ, $P < 0.001$ (D). Peak torque during the test trains was used to set stimulation intensity.

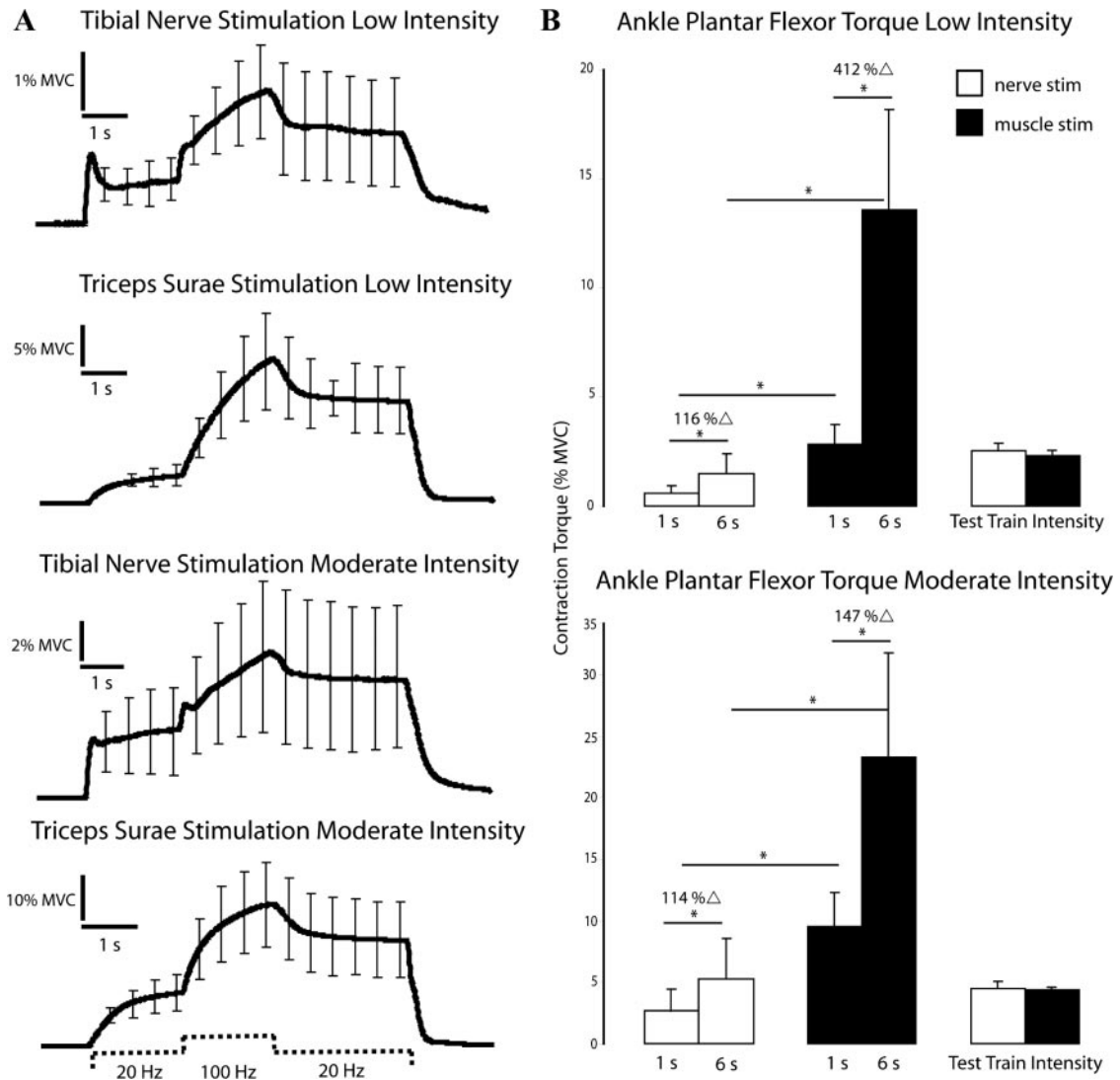


Fig. 3. Group average torque (A) during 7-s burst stimulation (stimulation profile depicted by dotted line) and comparisons between torques during initial and subsequent 20-Hz stimulation periods (B) for tibial nerve and triceps surae stimulation at low and moderate intensities. *Significant torque differences. Muscle stimulation at low and moderate intensities produced significantly larger absolute torques during initial ($P = 0.0002$ and $P = 0.003$, respectively) and subsequent 20-Hz stimulation periods ($P = 0.0002$ and $P = 0.002$, respectively) compared with nerve stimulation at comparable intensities. Significant extra contractions were produced with nerve stimulation at low ($P = 0.022$) and moderate ($P = 0.03$) intensities and with muscle stimulation at low ($P = 0.0002$) and moderate ($P = 0.0007$) intensities. stim, Stimulation.

significant extra contractions in all subjects, and group torque increased significantly from 9.4 (SD 4.2) to 22.3 (SD 11.7) %MVC. Significant main effects were found for stimulation type [$F(1,9) = 25.4, P = 0.0007$] and intensity [$F(1,9) = 10.85, P = 0.009$] on group plantar flexion torque difference values between the initial and subsequent 20-Hz stimulation periods. Muscle stimulation produced significantly greater torque differences than nerve stimulation, and hence larger extra contractions. Similarly, significantly larger extra contractions were produced with moderate- compared with low-intensity stimulation.

Wrist flexors. Torque profiles of five successive burst stimulations, produced during nerve and muscle stimulation at both low and moderate intensities, are shown for a single subject in Fig. 4. In this subject, significant extra contractions were produced by three of four stimulation types; relative torque increased from 1.3 to 3.2% MVC during nerve stimulation

(Fig. 4A) at a low stimulation intensity; and from 5.7 to 7.9% MVC and 4.9 to 6.9% MVC during nerve (Fig. 5C) and muscle (Fig. 5D) stimulation, respectively, at a moderate stimulation intensity. Low-intensity muscle stimulation (Fig. 4B) did not produce significant extra contractions as torque increased slightly from 2.2 to 2.4% MVC. Qualitatively, the shapes of the torque profiles for nerve and muscle stimulation appear similar to one another, as both show a smooth increase in torque at the onset of stimulation.

Group data for stimulation of the wrist flexors are displayed in Fig. 5. As indicated in the single-subject data (Fig. 4A), the shapes of the torque profiles between stimulation types are similar in the wrist flexors (Fig. 5A). Absolute torque produced during subsequent 20-Hz stimulation periods was not statistically different between nerve and muscle stimulation at the low [2.5 (SD 1.8) and 3.7 (SD 3.3) %MVC, respectively] or moderate intensity [7.2 (SD 4.3) and 10.9 (SD 8.7) %MVC,

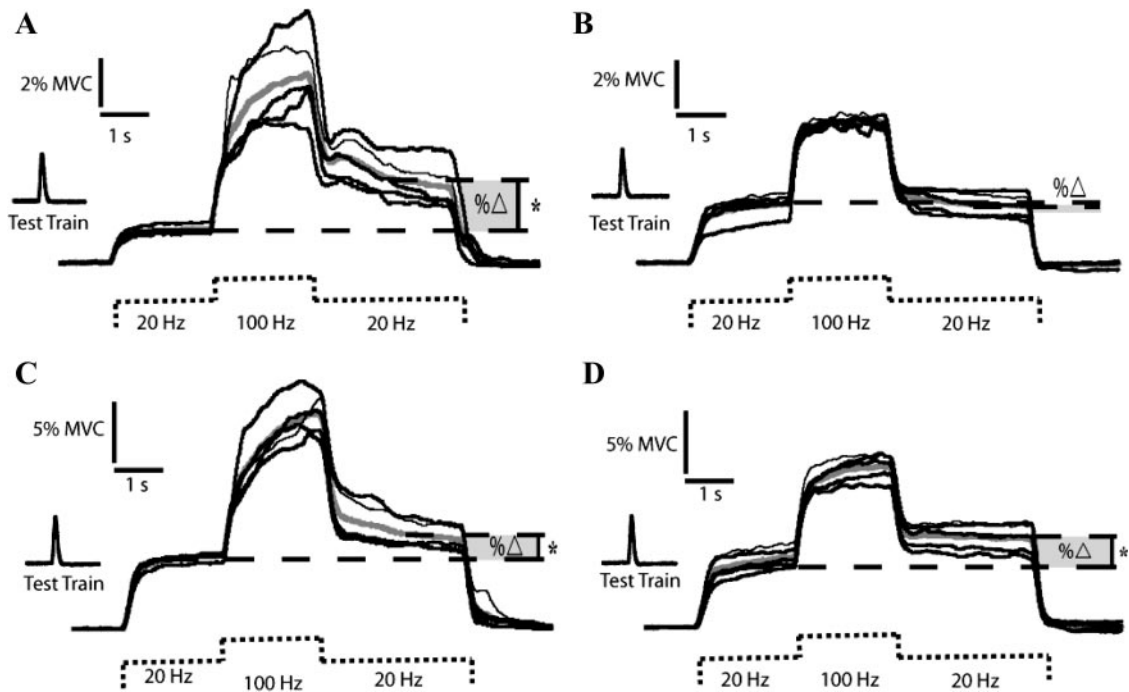


Fig. 4. Torque recorded from a single subject during median nerve and wrist flexor stimulation at low (A and B) and moderate (C and D) stimulation intensities. Gray traces denote the mean of the 5 torque profiles (black traces). Gray regions between dashed lines represent the amount the torque increased from before to after the 100-Hz stimulation period (% Δ). *Significant torque increases: 153 % Δ , $P = 0.003$ (A); 10 % Δ , $P = 0.59$ (B); 40 % Δ , $P = 0.013$ (C); and 42 % Δ , $P = 0.016$ (D).

respectively]. Low-intensity nerve and muscle stimulation of the forearm flexors produced significant extra contractions in 7 of 10 individuals and yielded significant increases in group torque from 1.7 (SD 1.4) to 2.5 (SD 1.8) %MVC and 2.5 (SD 1.9) to 3.7 (SD 3.3) %MVC, respectively. Moderate-intensity nerve stimulation produced significant extra contractions in 8 of 10 individuals and significantly increased group torque from 5.2 (SD 3.3) to 7.2 (SD 4.3) %MVC. Moderate-intensity muscle stimulation produced significant extra contractions in 9 of 10 individuals, and torque significantly increased from 6.6 (SD 4.4) to 10.9 (SD 8.7) %MVC across the group. A significant main effect was found for stimulation intensity [$F(1,9) = 6.06$, $P = 0.04$] in the wrist flexors, where significantly larger torque differences were produced with moderate- compared with low-intensity stimulation. There were no significant differences in the amplitude of torque differences between nerve and muscle stimulation.

Plantar flexors vs. wrist flexors. The changes in torque produced by the stimulation, assessed by the difference in torque between the initial and subsequent 20-Hz stimulation periods, varied between muscle and nerve stimulation in the plantar flexors and wrist flexors as seen by comparing Figs. 3 and 5. At the low stimulation intensity, main effects for muscle group [$F(1,9) = 32.5$, $P = 0.0003$] and stimulation type [$F(1,9) = 26.0$, $P = 0.0006$], along with a significant interaction between muscle group and stimulation type [$F(1,9) = 31.2$, $P = 0.0003$], were detected. The torque differences in the plantar flexors [10.6 (SD 5.7) %MVC] were greater than those produced in the wrist flexors [1.2 (SD 1.4) %MVC] with low-intensity muscle stimulation ($P = 0.0003$) but were similar between the plantar flexors [0.9 (SD 1.0) %MVC] and wrist flexors [0.8 (SD 0.8) %MVC] with low-intensity nerve

stimulation. Main effects for muscle group [$F(1,9) = 5.9$, $P = 0.04$] and stimulation type [$F(1,9) = 29.2$, $P = 0.0004$], along with a significant interaction between muscle group and stimulation type [$F(1,9) = 6.2$, $P = 0.03$], were identified for moderate-intensity stimulation. Similar to low-intensity stimulation, torque differences in the plantar flexors [13.8 (SD 8.6) %MVC] were greater than those produced in the wrist flexors [4.2 (SD 4.6) %MVC] with moderate-intensity muscle stimulation ($P = 0.02$) but were similar between the plantar flexors [2.6 (SD 3.2) %MVC] and wrist flexors [2.0 (SD 1.7) %MVC] with moderate-intensity nerve stimulation. In the plantar flexors, greater torque differences were produced with muscle stimulation, compared with nerve stimulation, at both low ($P = 0.0002$) and moderate ($P = 0.008$) intensities. In the wrist flexors, the differences in torque produced were similar between stimulation types at both intensities.

Consistency Between Contractions

Plantar flexors. To assess the consistency between contractions, the CV between contractions produced during five consecutive burst stimulations, in the subsequent 20-Hz stimulation periods, was calculated for nerve and muscle stimulation at both intensities (see Fig. 6A). Across the group, there were significant main effects for stimulation type [$F(1,9) = 33.58$, $P = 0.0003$] and intensity [$F(1,9) = 6.45$, $P = 0.03$] on the consistency of consecutive contractions. A significant interaction between stimulation type and intensity [$F(1,9) = 6.25$, $P = 0.03$] was present also. Post hoc analyses revealed contraction consistency (Fig. 6B) was similar between moderate-intensity nerve [CV: 0.2 (SD 0.1)] stimulation and muscle stimulation at low [CV: 0.1 (SD 0.04)] and moderate [CV: 0.1

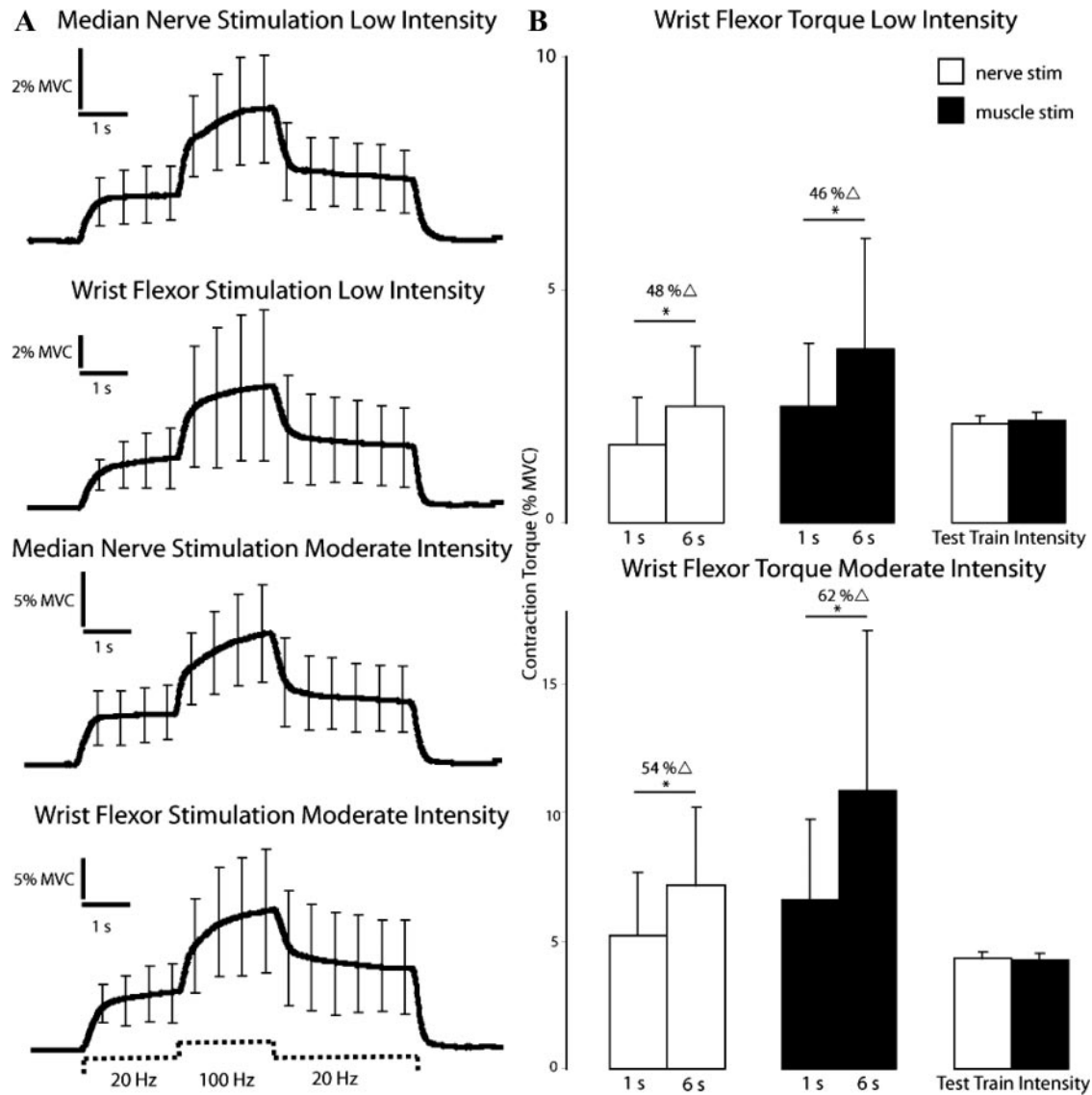


Fig. 5. Group average torque traces (A) during 7-s burst stimulation pattern (stimulation profile depicted by dotted line) and direct comparisons between torques during initial and subsequent 20-Hz stimulation periods (B) for median nerve and wrist flexor stimulation at low and moderate stimulation intensities. *Significant torque differences. Absolute torque was not statistically different between nerve and muscle stimulation at either intensity. Significant relative torque increases (extra contractions) were produced with nerve stimulation at low ($P = 0.007$) and moderate ($P = 0.005$) intensities and with muscle stimulation at low ($P = 0.023$) and moderate ($P = 0.02$) intensities.

(SD 0.04) intensities. Low-intensity nerve stimulation [CV: 0.5 (SD 0.3)] produced contractions that were significantly more variable than moderate-intensity nerve stimulation and muscle stimulation at low and moderate intensities.

Wrist flexors. Across the group, contraction consistency was similar for nerve and muscle stimulation at low [CV: 0.3 (SD 0.2) and 0.2 (SD 0.1), respectively] and moderate [CV: 0.2 (SD 0.1) and 0.2 (SD 0.1), respectively] intensities since no significant main effects were detected (Fig. 6C).

Stability Within Contractions

Ankle plantar flexors. To assess the stability of the torque produced within a contraction, the CV of each contraction profile over the last 2 s of the subsequent 20-Hz stimulation periods was calculated (Fig. 7A). Stimulation of the ankle

plantar flexors yielded a significant main effect for stimulation type [$F(1,9) = 5.80, P = 0.04$]. Contraction stability (Fig. 7B) was similar within each type of stimulation, irrespective of intensity. Moderate-intensity nerve stimulation [CV: 0.08 (SD 0.06)] and muscle stimulation at low [CV: 0.03 (SD 0.05)] and moderate [CV: 0.03 (SD 0.03)] intensities were also similar; however, low-intensity nerve stimulation [CV: 0.3 (SD 0.3)] was significantly less stable than muscle stimulation at both intensities.

Wrist flexors. Similar to contraction consistency, there were no significant main effects for stimulation type or intensity in the wrist flexors across the group (Fig. 7C). Contraction stability was similar for low [CV: 0.07 (SD 0.04)] and moderate [CV: 0.05 (SD 0.04)] nerve stimulation, as well as low [CV: 0.07 (SD 0.04)] and moderate [CV: 0.05 (SD 0.01)] muscle stimulation.

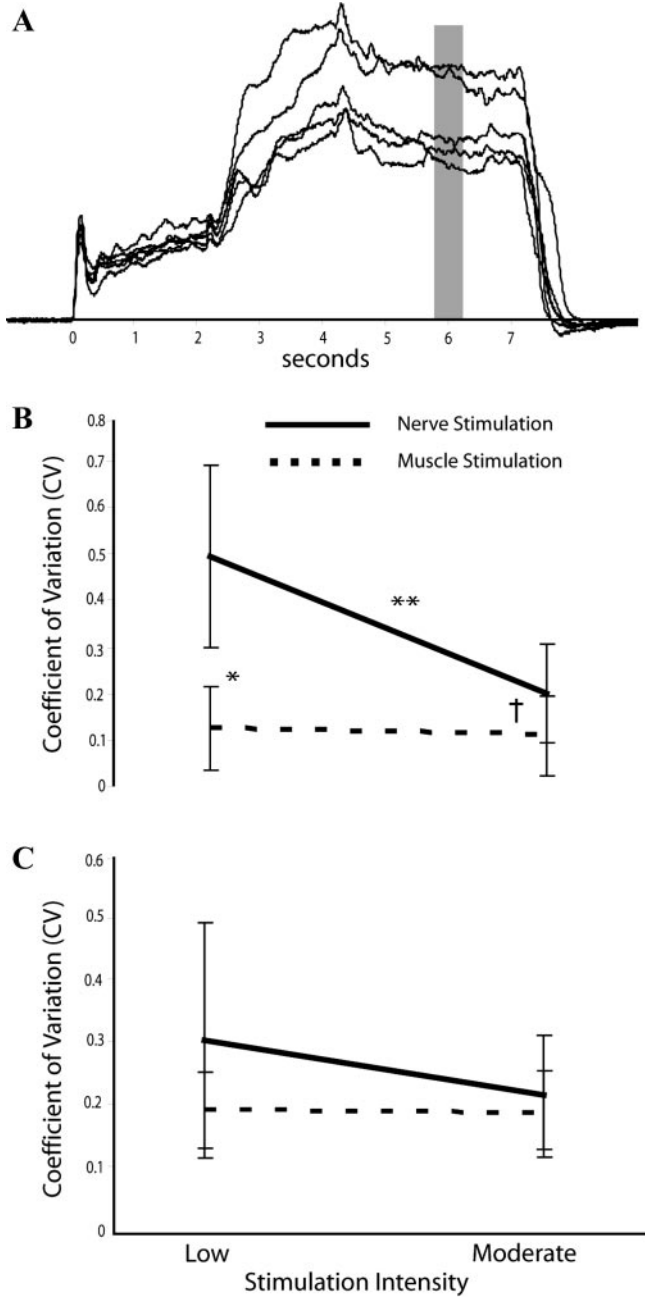


Fig. 6. A: contraction consistency as measured by the coefficient of variation (CV) between 5 consecutive burst stimulation torque profiles during subsequent 20-Hz stimulation periods. B: in the plantar flexors, low-intensity nerve stimulation was significantly less consistent than at the moderate intensity (** $P = 0.01$) as well as low- (* $P = 0.005$) and moderate-intensity ($\dagger P = 0.003$) muscle stimulation. C: in the wrist flexors, contraction consistency was similar for nerve and muscle stimulation at both low and moderate intensities. Solid and dashed lines indicate nerve and muscle stimulation, respectively.

M Waves and H Reflexes

M-wave and H-reflex responses were recorded to assess potential peripheral and central contributions to the extra contractions. Raw EMG traces during low-intensity nerve and muscle stimulation, in the lower and upper limb, for a single subject are presented in Fig. 8. Traces show data over a 400-ms window, 200 ms on either side of 1 s, during the initial 20-Hz

stimulation period in a single-burst stimulation pattern. These data demonstrate the presence of H reflexes during nerve stimulation (Fig. 8, A and C) and their absence during muscle stimulation (Fig. 8, B and D). In the soleus, H reflexes were larger than M waves during tibial nerve stimulation (Fig. 8A) and were absent during muscle stimulation (Fig. 8B). Across the four subjects analyzed, soleus H reflexes [1.7 (SD 1.7) % M_{max}] were 3.4 times larger than M waves [0.5 (SD 0.3)

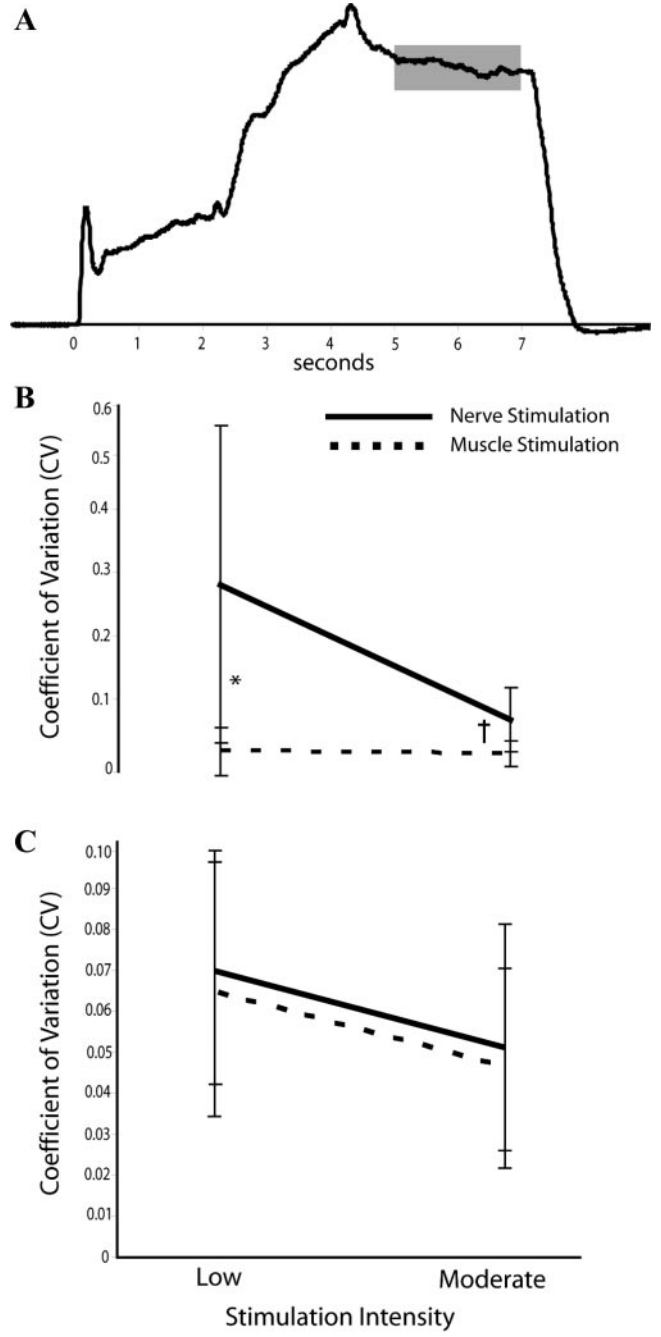


Fig. 7. A: contraction stability as measured by the CV over the last 2 s of stimulation. B: in the plantar flexors, low-intensity nerve stimulation was significantly less stable than muscle stimulation at low (* $P = 0.03$) and moderate ($\dagger P = 0.03$) intensities. C: in the wrist flexors, contraction stability was similar for nerve and muscle stimulation at both low and moderate intensities. Solid and dashed lines indicate nerve and muscle stimulation, respectively.

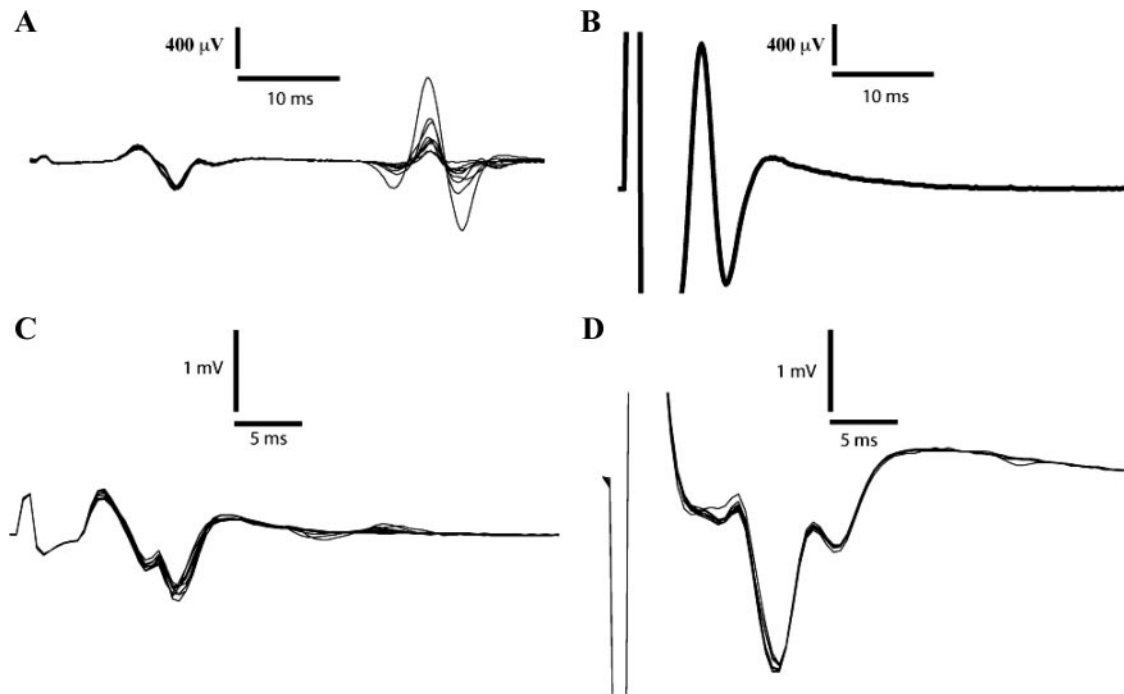


Fig. 8. Raw electromyograph traces during low-intensity tibial nerve (A), triceps surae (B), median nerve (C), and wrist flexor (D) stimulation in a single subject. Traces shown were collected during a 400-ms window spanning 200 ms before and after the 1-s mark of a burst stimulation pattern (during the initial 20-Hz stimulation period). Traces demonstrate the absence of H reflexes and dominance of M waves during muscle stimulation compared with nerve stimulation at a similar intensity. Additionally, H reflexes were far less frequent and M waves were more prominent during nerve stimulation of the wrist flexors compared with plantar flexors. Artifacts are truncated in the muscle stimulation traces (B and D).

$\%M_{\max}$] during tibial nerve stimulation. Conversely, M waves [21 (SD 16) $\%M_{\max}$] were an average of 15 times larger than H reflexes [1.4 (SD 1.0) $\%M_{\max}$] in the same four subjects during triceps surae stimulation. In the wrist flexors (Fig. 8C), H reflexes were less frequent and M waves more dominant during nerve stimulation, yet, similar to the plantar flexors, M waves remained during muscle stimulation, whereas H reflexes were reduced (Fig. 8D). Across the three subjects analyzed, M waves [17 (SD 8.5) $\%M_{\max}$] were 8.5 times larger than H reflexes [2.0 (SD 1.7) $\%M_{\max}$] during median nerve stimulation. During muscle stimulation in the same three subjects, M waves [37 (SD 23.6) $\%M_{\max}$] were an average of 18.5 times larger than H reflexes [2.0 (SD 1.4) $\%M_{\max}$]. H_{\max} -to- M_{\max} ratios calculated from the recruitment curves demonstrated significantly larger H_{\max} values for a given M_{\max} in the plantar flexors compared with the wrist flexors ($P = 0.0004$). H_{\max} -to- M_{\max} ratios were 0.70 (SD 0.14) and 0.23 (SD 0.18) for the plantar and wrist flexors, respectively.

DISCUSSION

This experiment was designed to identify the most effective method of delivering high-frequency, wide-pulse-width stimulation to evoke contractions enhanced through spinal pathways (extra contractions) for NMES. To be useful for NMES, the torque produced by the extra contractions should be large, consistent between successive contractions, and stable within each contraction. In the triceps surae, muscle stimulation produced contractions that were larger (up to 23% MVC), evoked the largest extra contractions since torque was four times greater than expected solely from direct motor axon activation, and were more consistent and stable compared with contrac-

tions produced by tibial nerve stimulation. In the wrist flexors, nerve and muscle stimulation were equally effective. Torques reached 11% MVC, and significant extra contractions produced up to 1.6 times more torque than expected from direct motor axon stimulation alone. This represents a new finding since the presence of extra contractions has not previously been reported in the wrist flexors. The ability to evoke extra contractions in the wrist flexors may be useful for electrical devices assisting upper limb motor function. Absolute torques, central contribution amplitudes, consistency, and stability of the evoked wrist flexor torques were similar between the stimulation types. Muscle stimulation produced the larger extra contractions in the plantar flexors compared with wrist flexors; however, the amplitude of the extra contractions was similar between the two muscle groups with nerve stimulation.

Implications

Applying the present stimulation parameters in rehabilitation devices could have several benefits. For example, if motor unit recruitment order follows Henneman's size principle, as would be expected for recruitment of motoneurons by Ia afferents (20), contractions should be more fatigue resistant than those generated by motor axon stimulation alone (10). This stimulation could also be used to treat muscle atrophy as it may recruit primarily slow-twitch muscle fibers not activated with conventional stimulation parameters (10). It may also be possible to reduce, reverse, or even prevent the transition from slow- to fast-twitch muscle fibers that accompanies a spinal cord injury. The stimulation may also assist in potentiating, or "warming-up," spinal motoneurons to assist in performing rhythmic tasks such as stepping during ambulatory training for

people with spinal cord injury. Warm-up, characterized by increased motor unit discharge through the activation of plateau potentials, is dependent on repetitive input to motoneurons (6, 15, 38, 42). This would be useful to “boost” motoneuron firing, and hence motor output, during repetitive/rhythmic tasks, such as walking, in a nervous system with impaired descending input. By using similar stimulation parameters to those used in this experiment, extra contractions were produced by stimulating over the triceps surae in 11 of 13 subjects with varying degrees of spinal cord injury, in some cases reaching 24% of the maximal stimulated contraction force (33). Given these results in persons with spinal cord injury, the stimulation parameters used in this study appear promising for integration into devices assisting with motor function. However, to restore movement and posture, the ability to not only reliably increase but also decrease the central contribution to the evoked torque would be essential. Reciprocal inhibition, induced by electrical stimulation of the antagonist (common peroneal) nerve, can “turn-off” the central contribution to soleus contractions during the stimulation (13) as well as the residual soleus muscle activity that often remains after the stimulation has ended (34). Thus stimulation applied to agonist and antagonist nerves will likely be required to achieve the control necessary for the restoration of posture and movement.

Nerve vs. Muscle Stimulation

A striking feature of the present results is the large extra contraction amplitudes evoked with muscle stimulation compared with nerve stimulation in the ankle plantar flexors. One difference between the two stimulation types for the plantar flexors is that M waves dominated responses during muscle stimulation and H reflexes dominated during nerve stimulation as shown in Fig. 8. Spinal pathways have been identified as an imperative component in generating extra contractions (10, 11), and the presence of H reflexes during high-frequency stimulation lends support to this idea (34). Further evidence for spinal contributions during extra torque production has been demonstrated previously in our laboratory, in which case soleus H reflexes during 20-Hz tibial nerve stimulation increased concurrently with torque after 2 s of 100-Hz stimulation with no change in M-wave amplitudes (27). This suggests that the extra contractions were not generated by changes in stimulation intensity or potentiation at the muscle level. Based on our data, it is difficult to attribute extra torque generation in the ankle plantar flexors entirely to spinal pathways when the M waves, a product of direct motor axon stimulation, appear to be driving the contractions during muscle stimulation. Similarly, in the wrist flexors, the EMG traces shown in Fig. 8, C and D, indicate M waves to be the prominent waveform during the 20-Hz stimulation. However, previous studies using muscle stimulation clearly show extra contractions are abolished during nerve block proximal to the stimulation site (10, 11), thus demonstrating the importance of afferent input to the spinal cord even during muscle stimulation. The predominance of M waves during muscle stimulation does not exclude a contribution from the discharge of spinal neurons to the torque output; however, it suggests this discharge may not be time-locked to the stimulus. Thus motor unit firing may be sustained through intrinsic membrane properties such as plateau potentials, triggered by the 100-Hz stimulation resulting in asynchronous

discharge patterns that become uncoupled from afferent input to the motoneuron pool. Asynchronously discharging motor units have previously been cited as a potential mechanism underlying the extra contractions (10, 11, 33) and have been observed during contractions evoked by electrical stimulation (9, 11, 29) and tendon vibration (9, 29). Thus enhanced H reflexes may contribute but may not be necessary for generating extra contractions, and the mechanisms may be specific to the type of stimulation used.

The prevalence of H reflexes and M waves during nerve and muscle stimulation in the plantar flexors, respectively, can be explained in part by differences in stimulation location. Stimulation over the muscle was delivered close to the motor point and, therefore, may have activated a greater proportion of motor rather than sensory axons at low stimulation intensities. As a result, M waves predominated during muscle stimulation. Conversely, stimulation over the nerve trunk, where sensory and motor axons are more evenly mixed, recruited a relatively greater proportion of sensory axons at low stimulation intensities, and H-reflexes were more prevalent.

The different contributions of H reflexes and M waves may have affected stimulation intensity matching during nerve and muscle stimulation in the plantar flexors. During nerve stimulation, H reflexes were 3.4 times larger than M waves; however, M waves were 15 times larger than H reflexes during muscle stimulation. In the individual (Fig. 2A) and group torque profiles (Fig. 3A), a sharp increase followed by a rapid decrease in torque can be clearly identified at the onset of stimulation. Experiments in our laboratory have demonstrated that a large H reflex (34% M_{max}), evoked by the first stimulus pulse of 20-Hz stimulation, can produce a concurrent torque response of 4% MVC (27). The large initial H reflex is attenuated thereafter, as is the torque, and is indicative of postactivation depression commonly observed during tetanic stimulation (9, 12, 23, 40, 43, 45). A large initial H reflex could account for the peak torque measured during nerve stimulation test trains. With muscle stimulation, the H reflex was absent, as was the initial torque deflection. Without the large initial H reflex during muscle stimulation, the torque produced during the test trains likely required greater amounts of current to achieve the torque evoked by nerve stimulation. Comparisons, however, between low-intensity muscle stimulation and moderate-intensity nerve stimulation, when the torques generated before the 100-Hz bursts were similar (see Fig. 3), demonstrate that muscle stimulation was still more effective in generating the largest extra contractions.

Lower vs. Upper Limb Stimulation

The extent to which extra contractions are present in forearm muscles had not previously been tested. Extra contractions were present in the wrist flexors as in the plantar flexors. However, differences between stimulation types observed in the ankle plantar flexors were absent in the wrist flexors. This may relate to the large influence of H reflexes on soleus contractions with nerve stimulation. During this experiment, H reflexes in the wrist flexors were small and their presence sporadic. The threshold to evoke H reflexes in flexor carpi radialis is typically at higher M wave amplitudes than in soleus and are therefore reduced in amplitude as a result of antidromic collision in the efferent axon (2). During low-intensity median

nerve stimulation, H-reflex amplitudes were much smaller (8.5 times) than concomitant M waves (see Fig. 8C) and less likely to influence torque output during the test trains. The compromised influence of the H reflex is demonstrated as the initial deflections in torque observed with tibial nerve stimulation (Fig. 4) are absent with median nerve stimulation (Fig. 5). Without the influence of the H reflex, fewer differences were likely observed between nerve and muscle stimulation in the wrist flexors because of improved intensity matching between them.

The magnitude of extra contractions evoked in the plantar flexors during low- and moderate-intensity muscle stimulation was nine and three times larger than contractions evoked in the wrist flexors at similar intensities. With nerve stimulation, extra contractions were slightly larger but not statistically different during low- and moderate-intensity stimulation between the lower and upper limb muscles tested. Greater levels of cortically imposed PSI on flexor carpi radialis Ia afferents, compared with soleus spindle (Ia) afferents have been observed in neurologically intact humans (32). The comparison of H_{\max} -to- M_{\max} ratios from our data supports this idea because H_{\max} was much smaller with respect to M_{\max} in the wrist flexors compared with the plantar flexors. Greater levels of PSI on wrist flexor Ia afferents could account for this difference. The 1-ms pulse widths used in this experiment were selected to preferentially activate Ia afferents (22, 36, 46), and their input to the spinal cord is imperative in producing the extra contractions (10). Thus PSI will have a very strong influence on the input received by the α -motoneuron and will greatly influence the resulting motor output. The absence of statistically different magnitudes of extra contraction between the plantar flexors and wrist flexors with nerve stimulation is not explained by varying degrees of PSI in the upper and lower limbs. It is possible that larger responses, evoked with higher nerve stimulation intensities, would more clearly demonstrate a difference between the upper and lower limb.

Mechanisms

Motoneurons, once thought of as passive integrators of synaptic input, are now known to possess intrinsic membrane properties, such as persistent inward currents generated by low-voltage activated Ca^{2+} channels and Na^{+} channels that produce sustained depolarizations and discharge that outlast the initial input (5, 19, 24, 41). Prolonged depolarizations caused by persistent inward currents are known as plateau potentials and have been suggested as one mechanism underlying extra contractions in studies similar to this one (10, 11). The extra contractions have been associated with plateau potentials because of their dependency on high-frequency input to the spinal cord through large-diameter afferents, in addition to residual EMG outlasting the stimulation and evidence of asynchronous motor unit discharge (10). Plateau potentials induced with high-frequency input have been demonstrated in animals (5, 30) and indirectly in humans using electrical stimulation (10, 11) and tendon vibration (16, 17, 25). High-frequency afferent input to the spinal cord is capable of recruiting motoneurons that fire autonomously, which is one hallmark of plateau potentials (16). The present data fit with the idea of plateau potentials occurring in motoneurons as the additional recruitment of motoneurons firing independent of stimulation

frequency could explain the increased torque we observed during the burst stimulations once the stimulation was reduced from 100 to 20 Hz.

Posttetanic potentiation (PTP) could also contribute to the extra contractions observed. Sources of PTP can be found both centrally and peripherally following repetitive electrical stimulation. Centrally, PTP at the Ia synapse results in the enhancement of excitatory postsynaptic potentials (21). Peripherally, PTP of the muscle fibers enhances torque profiles (35). A proposed mechanism for PTP at the Ia synapse is a reduced probability of failure to release neurotransmitter from the presynaptic membrane, coupled with an increased likelihood of multi-quantal release (21). Repetitive stimulation of Ia afferents has been shown to facilitate enhancement of excitatory postsynaptic potentials of motoneurons and may be one factor in maintaining motoneuron excitability (21). Alternatively, PTP of the muscle fiber is attributed to greater myosin light chain phosphorylation caused by increased Ca^{2+} release from the sarcoplasmic reticulum (1, 14, 18).

From the data collected in this experiment, it is difficult to ascertain which mechanism was the prime contributor to the extra contractions. However, PTP of the muscle fibers seems least likely since previous studies have shown an absence of the extra contractions during nerve block (10). If PTP of the muscle fibers was a factor in generating the extra contractions, one would expect to see the characteristic torque increases even in the absence of input from spinal neurons. It therefore seems likely mechanisms underlying the extra contractions are spinal in origin. Whether the specific mechanism is plateau potentials, PTP at the Ia synapse, or a combination of the two remains unclear.

In conclusion, the implementation of high-frequency, wide-pulse-width stimulation parameters has been suggested for use in NMES rehabilitation modalities such as functional electrical stimulation (FES) (10, 11). This experiment is an initial step toward implementing such an idea. The results demonstrate that, when stimulating the ankle plantar flexors, muscle stimulation produces larger peak torques and that the greatest extra contractions are more consistent between contractions and stable within a contraction compared with nerve stimulation. Moderate-intensity muscle stimulation was effective in generating the largest absolute torques; however, the largest extra contractions (relative torques) were produced with low-intensity muscle stimulation. When the wrist flexors were stimulated, extra contractions were evoked with each type of stimulation, but peak amplitudes, extra contractions magnitudes, consistency, and stability were similar between them. Based on the EMG data, nerve and muscle stimulation of the plantar flexors may operate through different neural pathways, although this requires confirmation in additional subjects. In the wrist flexors, the pathways responsible for producing the extra contractions were similar. This study is the first to demonstrate the presence of extra contractions in the forearm muscles, an important finding given that FES is often used to stimulate muscles acting about the wrist to assist in grasping tasks. Many factors are yet to be evaluated with respect to using these stimulation parameters in FES applications. Future work will need to focus on the assessment of motor unit recruitment to test the hypothesis that motor units recruited through central pathways during the extra contractions are slow twitch in nature. Additionally, the assessment of extra contraction fa-

tigue compared with contractions evoked by conventional stimulation parameters, and the capability of extra contractions assisting in the completion of functional tasks, should be explored as well. We propose that high-frequency, wide-pulse-width electrical stimulation may reduce the rapid muscle fatigue associated with current FES technologies and improve muscle atrophy treatment by recruiting muscles fibers not normally activated by electrical stimulation.

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