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Turning on the central contribution to contractions evoked by neuromuscular electrical stimulation

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Dean JC, Yates LM, Collins DF. Turning on the central contribution to contractions evoked by neuromuscular electrical stimulation. *J Appl Physiol* 103: 170–176, 2007. First published April 26, 2007; doi:10.1152/japplphysiol.01361.2006.—Neuromuscular electrical stimulation can generate contractions through peripheral and central mechanisms. Direct activation of motor axons (peripheral mechanism) recruits motor units in an unnatural order, with fatigable muscle fibers often activated early in contractions. The activation of sensory axons can produce contractions through a central mechanism, providing excitatory synaptic input to spinal neurons that recruit motor units in the natural order. Presently, we quantified the effect of stimulation frequency (10–100 Hz), duration (0.25–2 s of high-frequency bursts, or 20 s of constant-frequency stimulation), and intensity [1–5% maximal voluntary contraction (MVC) torque generated by a brief 100-Hz train] on the torque generated centrally. Electrical stimulation (1-ms pulses) was delivered over the triceps surae in eight subjects, and plantar flexion torque was recorded. Stimulation frequency, duration, and intensity all influenced the magnitude of the central contribution to torque. Central torque did not develop at frequencies ≤20 Hz, and it was maximal at frequencies ≥80 Hz. Increasing the duration of high-frequency stimulation increased the central contribution to torque, as central torque developed over 11 s. Central torque was greatest at a relatively low contraction intensity. The largest amount of central torque was produced by a 20-s, 100-Hz train (10.7 ± 5.5 %MVC) and by repeated 2-s bursts of 80- or 100-Hz stimulation (9.2 ± 4.8 and 10.2 ± 8.1% MVC, respectively). Therefore, central torque was maximized by applying high-frequency, long-duration stimulation while avoiding antidromic block by stimulating at a relatively low intensity. If, as hypothesized, the central mechanism primarily activates fatigue-resistant muscle fibers, generating muscle contractions through this pathway may improve rehabilitation applications.

plateau potentials; posttetanic potentiation; recruitment order; rehabilitation

NEUROMUSCULAR ELECTRICAL STIMULATION (NMES) can elicit contractions by direct activation of motor axons (generating peripheral torque about a joint) or through a central mechanism in which motoneurons in the spinal cord are recruited by the evoked sensory volley (generating central torque) (7, 8). Direct motor axon activation recruits motor units either in a random order (17) or by first activating fast fatigable muscle fibers (11). In contrast, synaptic activation recruits motor units in their natural order, starting with fatigue resistant muscle fibers (20). Thus generating muscle contractions through the central mechanism may be beneficial for decreasing muscle atrophy (therapeutic electrical stimulation), because the primary cause of atrophy is the disuse-related loss of fatigue-resistant fibers (16). The central mechanism may also assist in the production of useful movements [functional electrical stimulation (FES)], which are often limited by the rapid onset of fatigue. The present experiments are designed to identify the stimulation patterns that maximize the torque produced through the central mechanism (see also Ref. 8).

Wide-pulse (~1 ms) electrical stimulation preferentially activates sensory axons (27, 31, 34) and provides excitatory synaptic input to motoneurons in the spinal cord. Tetanic stimulation using wide pulses delivered at a constant high frequency (7, 8, 29) or as brief "bursts" of high-frequency pulses (1, 7, 8, 25, 29) generates larger torques than would be expected from direct motor axon activation alone. These torques are attributed to an involuntary central mechanism, because the increased torque was not present when a nerve block was applied proximal to the stimulation site (7, 8), but it was present in complete spinal cord-injured (7, 29) and healthy sleeping subjects (7). Therefore, Collins and colleagues (7, 8) have proposed that central torque is initiated by the evoked sensory volley that provides an excitatory input to neurons in the spinal cord.

This synaptic drive results in a slowly developing contraction that could be due to increased motoneuron firing through a presynaptic or postsynaptic mechanism. High-frequency (~200 Hz) repetitive stimulation of a sensory nerve can increase neurotransmitter release from Ia terminals [posttetanic potentiation (PTP)] (21), thereby increasing motoneuron activation and torque. Alternatively, the sensory volley may generate persistent inward currents (PICs) in motoneurons through the opening of voltage-activated Ca^{2+} and Na^{+} channels (2, 3, 14, 15, 23). PICs produce sustained depolarizations (plateau potentials) that can result in self-sustained motoneuron discharge and may contribute to central torque and the residual muscle contraction that can follow periods of vibration (13, 24) or electrical stimulation (7, 8). High-frequency stimulation may initiate PTP or activate plateau potentials, and either mechanism may account for the association of increased torque with larger Hoffman (H) reflexes (25). Central torque is associated with motor unit discharge time locked to each stimulus pulse (25) as well as discharge that is not time locked with the electrical stimulation (7).

Presently, we proposed that the central torque would scale with the excitation of motoneurons through synaptic input from sensory axons. Therefore, to maximize central torque, the stimulation should generate the largest afferent volley, while minimizing the number of motoneurons that cannot contribute to central torque due to antidromic block in motor axons.

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Previously, Collins and colleagues demonstrated that wide-pulse (~1 ms) high-frequency (100 Hz) stimulation is particularly effective in activating the central mechanism (8). In the present study, we further examined the effect of surface NMES stimulation parameters (frequency, duration, and intensity) on the central contribution to torque using patterns of *1*) constant-frequency stimulation and *2*) burstlike patterns in which the frequency alternated between periods of low-frequency stimulation (20 Hz) and "bursts" of higher frequency stimulation (40–100 Hz). With increased stimulation frequency, sensory axons fire at a higher rate, producing greater temporal summation. Therefore, we expected higher frequencies to generate a larger excitatory input and to produce greater central torques. At a constant stimulation frequency, increasing the duration will increase the number of sensory action potentials produced. We hypothesized that longer stimulation durations would be associated with a cumulative effect, producing a greater excitatory input to the spinal cord and larger central torques. Finally, we anticipated that stimulation intensity would have a nonlinear effect on the magnitude of the central torque, because higher intensities would activate more sensory axons, but that it will also lead to greater antidromic block of motoneurons and hence reduce the effectiveness of the sensory input. Portions of these data have been presented previously in abstract form (9).

MATERIALS AND METHODS

Subjects

Experiments were conducted on eight volunteer healthy adult subjects (6 men, 2 women) ranging in age from 21 to 43 yr. All subjects completed written informed consent before participation in the study. The experiments were approved by the University of Alberta Health Research Ethics Board and were conducted in accordance with the Declaration of Helsinki.

Experimental Set-up

Subjects were seated on the chair of a Biodex dynamometer (System 3, Biodex Medical Systems, Shirley, NY) with their right hip flexed to 110°, their right knee flexed to 120°, their right ankle at 90°, and the lateral malleolus aligned with the axis of the dynamometer. The subject's trunk was at an approximate angle of 20° reclined from the vertical. We examined the activation of the central mechanism in the triceps surae, which has previously been reported to produce central torque (1, 7, 8, 25, 29).

Isometric plantar flexion torque was sampled at 2,000 Hz and stored on a computer for subsequent analysis. Flexible 4-cm-wide stimulating electrodes (Electrosurgical Patient Plate 1180: Split, 3M Health Care, St. Paul, MN) were placed across proximal and distal aspects of the right triceps surae. The proximal electrode was placed over the gastrocnemius at the point of approximately the largest circumference. The distal electrode was placed over the soleus, just below the bottom of the gastrocnemius muscle belly. The lengths of the electrodes (~15 cm and 10 cm for the proximal and distal electrodes, respectively) were adjusted to maximize the contact area. The activation of other muscles of the lower leg was avoided through visual inspection and palpation of these muscles during stimulation. If any contractions were detected, the electrode placement was adjusted.

Maximum Voluntary Contractions

Subjects completed several submaximal plantar flexion contractions before collecting maximum voluntary contraction (MVC) data. Subjects performed MVCs of the plantar flexors for 5 s, following instructions to "push down as if you were pressing a gas pedal, rapidly increase force to a maximum and hold this contraction." Each subject completed between two and four MVCs, separated by 2 min of rest, until the MVC torques varied by <10%. The MVC was quantified as the maximum torque achieved across trials during the time period starting 1 s after the start of the contraction, with an average value across subjects of 114.2 ± 35.1 N·m. The subject then received a series of electrical stimulation patterns as described below.

NMES

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) was used to deliver rectangular 1-ms electrical pulses to the triceps surae in varying stimulation patterns.

Test trains. A 5-pulse, 100-Hz "test train" (Fig. 1*A*) was used to set contraction intensity throughout the experiment by adjusting stimulation current to elicit a peak torque of 1, 3, or 5% of the torque produced during an MVC. These contraction intensities were chosen based on pilot work indicating that they are optimal for generating central torque. Three test trains, separated by 5 s, were delivered at the beginning of each trial, 5 s before the subsequent constant-frequency or burst-pattern train. The torque produced by the test trains was monitored to ensure that fatigue did not occur. This torque did not decline during the session.

Constant frequency. Constant-frequency trains of 20-s duration (Fig. 1*B*) were used to examine the effect of stimulation frequency and intensity on the magnitude and time course of central torque. Previous studies reported that plateau potentials can "warm up" over a period of 4–6 s (2, 15, 33), implying that 20 s should be sufficient time for

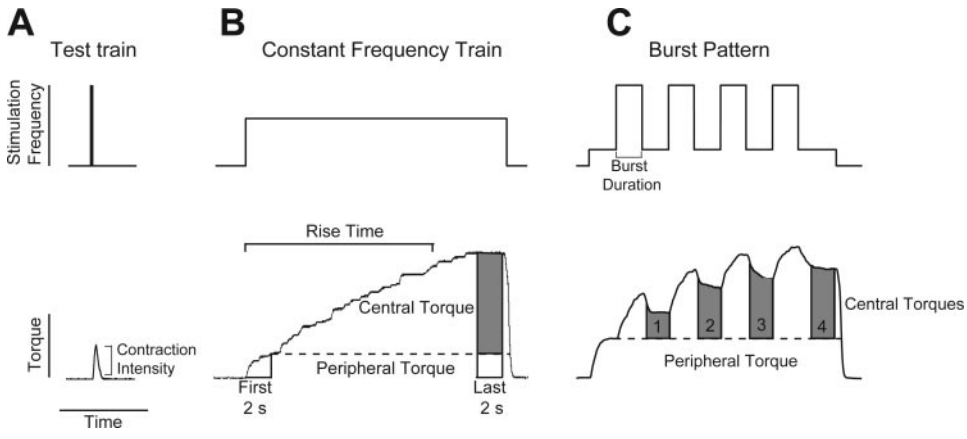

Fig. 1. Examples of the 3 stimulation patterns used in this study and sample torque traces from each. *A*: 5-pulse 100-Hz train was used to standardize the contraction intensity, by setting the torque to a percentage of the maximal voluntary contraction (MVC). *B*: effects of stimulation frequency and intensity were examined using 20-s constant-frequency trains. Peripheral torque, central torque (shaded region), and rise time were quantified. Rise time was calculated as the time to reach 90% of the peak torque value. *C*: effects of high-frequency stimulation bursts were quantified while varying the burst frequency, burst duration, and contraction intensity. The amount of peripheral torque and the central torque (shaded regions) produced following each burst was measured.

any central torque due to plateau potentials to develop. Stimulation frequencies of 10, 20, 50, and 100 Hz were delivered at intensities that evoked 1 and 3% MVC during a test train.

Burst patterns. "Burst patterns" were used to examine the effect of burst frequency, burst duration, and contraction intensity on central torque. The burst patterns consisted of four "bursts" of high-frequency stimulation, separated by 2-s periods of 20-Hz stimulation (Fig. 1*C*) and ending with a 3-s period of 20-Hz stimulation. The total duration of the burst patterns varied from 12 to 19 s. Pilot studies indicated that following four bursts, additional bursts did not produce more central torque. We tested the effect of frequency by applying bursts of 40-, 60-, 80-, or 100-Hz pulses for 2 s at a contraction intensity of 3% MVC. The effect of burst duration was examined by delivering 100-Hz bursts for 0.25, 0.5, 1.0, or 2.0 s at an intensity of 3% MVC. The effect of contraction intensity was tested by setting the intensity to 1, 3, or 5% MVC at a burst frequency and duration of 100 Hz and 2 s, respectively.

Subjects received each variation of the constant-frequency and burst-pattern trials three times, separated by 90 s of rest between stimulation trains and 2 min of rest between trials. Each testing condition was separated by 2 min of rest. The order of the trials was randomized for each subject. During all trials, subjects were instructed to remain relaxed during the stimulation. Each data collection session consisted of 57 stimulated tetanic contractions and lasted ~2 h.

Data Analysis and Definitions

Plantar flexion torque was normalized to each subject's MVC. Following a method adapted from Collins and colleagues (1, 7, 8), peripheral torque was quantified as the most consistent torque level produced during the first 2 s of stimulation (see Fig. 1, *B* and *C*). Central torque during constant-frequency stimulation was calculated as the additional torque produced during the final 2 s of stimulation (shaded region in Fig. 1*B*). Central torque during burst pattern stimulation was quantified as the additional torque during the periods of 20-Hz stimulation after each burst (shaded *regions 1–4* in Fig. 1*C*). To quantify the torque produced during a given time period, we calculated the average torque during the most stable region of that period (defined as the 0.5-s interval with the smallest coefficient of variation). The rise time of central torque development was quantified in the constant-frequency trials by calculating the time required to reach 90% of the peak torque value (Fig. 1*B*).

Statistics

Repeated-measures ANOVAs with a significance level of 0.05 were performed to test whether each stimulation pattern produced significant central torque, both in individuals and in the group data. Central torque was determined to be significant when it was significantly greater than zero. Therefore, a subject could have an average central torque greater than zero but not significantly different from zero. Repeated-measures ANOVAs were also used to test for significant effects of the stimulation parameters on central torque magnitude and rise time. For the constant-frequency trains, the independent factors were stimulation frequency and contraction intensity. For the burst patterns, the number of bursts delivered was one independent factor, and the stimulation parameter (burst frequency, burst duration, or contraction intensity) was the other independent factor. Tukey-Kramer post hoc tests with a significance level of 0.05 were performed where any significant main effects were found. Data are reported as means ± SD.

RESULTS

In seven of eight subjects, patterns of wide-pulse electrical stimulation generated significant central torque through reflexive inputs to the spinal cord in addition to the peripheral torque produced by direct motor axon activation. Constant-frequency stimulation (≥50 Hz) produced central torque, as did brief bursts of stimulation (≥40 Hz) alternating with 20-Hz stimulation. The magnitude of the central torque was influenced by the number of bursts, the burst frequency, the burst duration, and the contraction intensity.

Constant Frequency

Plantar flexion torque increased during constant-frequency stimulation for 20 s at or above 50 Hz (Fig. 2*A*). The largest central torques were generated with 100-Hz stimulation (9.6 ± 7.1% MVC, range 0.0–18.9% MVC with a contraction intensity of 1% MVC; 10.7 ± 5.5% MVC, range 6.5–22.1% MVC with a contraction intensity of 3% MVC). Constant-frequency 50- and 100-Hz stimulation generated significant central torque ($P < 0.05$), whereas 10- and 20-Hz stimulation did not (Fig. 2*B*). The amount of central torque produced with 100-Hz stimulation was significantly more than with 50-Hz stimulation ($P < 0.05$). Contraction intensity did not significantly affect central torque. With the higher frequencies that produced significant central torque (≥50 Hz), the average rise time was 11.4 ± 4.3 s (range 3.2–16.6 s). This measure did not vary significantly across frequency or intensity.

Burst Patterns

Bursts of high-frequency pulses during constant low-frequency stimulation generated significant sustained increases in

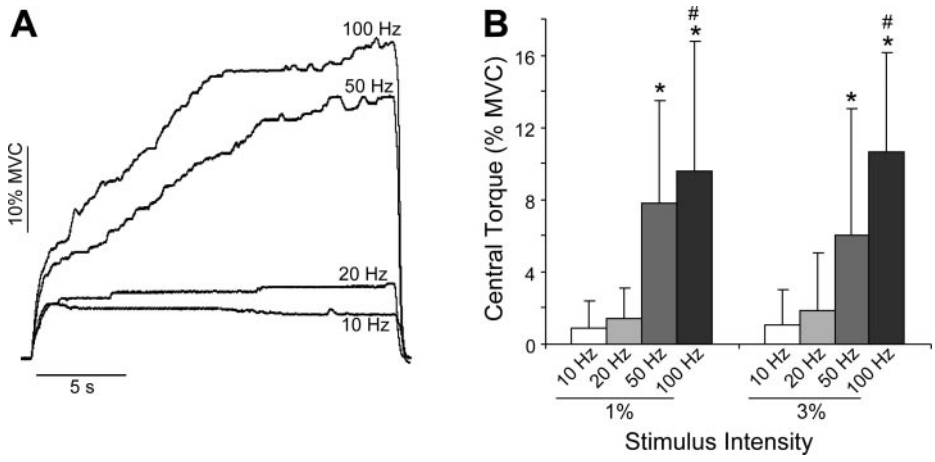

Fig. 2. Plantar flexor torque increased significantly during patterns of constant high-frequency (≥50 Hz) stimulation. *A*: single-subject data illustrating the gradual torque increase over time in response to a single stimulation train. *B*: significant extra torque was generated at 50 and 100 Hz but not at 10 or 20 Hz (*$P < 0.05$). The 100-Hz stimulation generated significantly more central torque than the 50-Hz stimulation (#$P < 0.05$). Contraction intensity did not have a significant effect on the development of central torque.

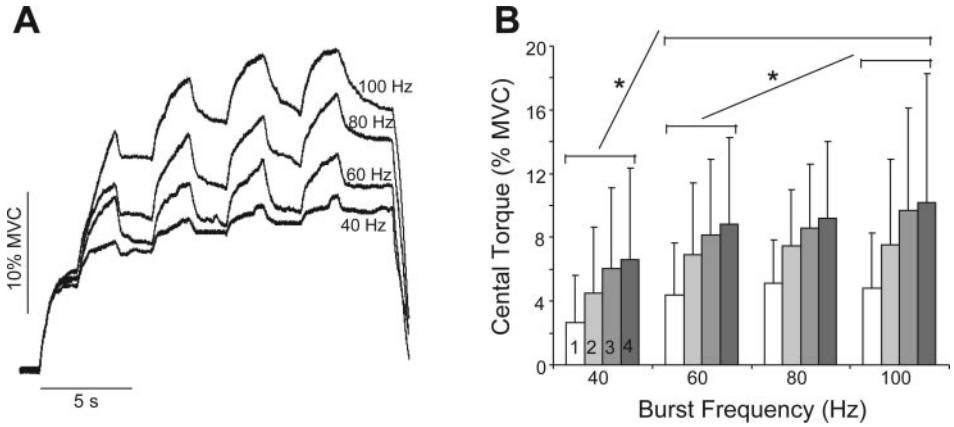

Fig. 3. Burst frequency had a significant effect on ankle torque. *A*: sample data for single-burst patterns in 1 subject illustrating the development of central torque following high-frequency bursts. *B*: number of bursts and burst frequency each significantly influenced central torque. The columns within each burst frequency (40, 60, 80, or 100 Hz) represent the central torque present following 1, 2, 3, and 4 bursts (see Fig. 1*C*). *Significant difference between indicated burst frequency groups, $P < 0.05$.

torque. Burst frequency, burst duration, contraction intensity, and the number of high-frequency bursts delivered influenced the magnitude of the central torque. The largest central torques produced by the burst patterns were not significantly different from the central torque produced by the 100 Hz constant frequency train.

The development of central torque was influenced by the stimulation frequency of the bursts. Higher frequencies produced larger central torques, as shown for a single subject in Fig. 3*A*. The central torque generated after four 40-Hz bursts (6.6 ± 5.7% MVC) was significantly less than that generated with higher frequency bursts (Fig. 3*B*). The largest central torques were produced by bursts of 80 or 100 Hz stimulation (9.2 ± 4.8% MVC, range 1.7–14.8% MVC; 10.2 ± 8.1% MVC, range −1.2–20.5% MVC). For all burst frequencies, a single burst generated significant central torque. The second and third bursts increased the central torque further, although the fourth burst did not have a significant effect at any frequency.

The central torque increased with the duration of the high-frequency bursts, as illustrated with single-subject data in Fig. 4*A*. Longer bursts generated significantly larger central torques, ranging from 2.8 ± 2.3% MVC after four 0.25 s bursts to 10.2 ± 8.1% MVC after four 2-s bursts (Fig. *4B*). For all durations, a single burst generated significant central torque. With longer burst durations (≥ 0.5 s), the second and third bursts increased the central torque, although the effect of the fourth burst was not significant.

Central torque also depended on contraction intensity. Although the peripheral torque varied with contraction intensity (first 2 s of the single-subject data presented in Fig. 5*A*), so did the magnitude of the central torque following the bursts (also shown in Fig. 5*A*). The peripheral torque scaled significantly ($P < 0.05$) with contraction intensity, as the lowest contraction intensity (1% MVC) generated an average peripheral torque of 1.7 ± 0.8% MVC, the intermediate intensity (3% MVC) generated 5.6 ± 2.9% MVC, and the highest intensity (5% MVC) generated 10.2 ± 3.5% MVC. However, the magnitude of the central torque was largest at the intermediate intensity (3% MVC). Following four bursts, the average magnitudes of the central torques were 7.0 ± 5.2, 10.2 ± 8.1, and 6.6 ± 7.0% MVC for the lowest contraction intensity, the intermediate intensity, and the highest intensity, respectively (Fig. *5B*). For all stimulus intensities, a single burst was sufficient to generate significant central torque. At lower intensities (1% and 3% MVC), the second and third bursts led to significant increases in central torque. Again, the fourth burst did not have a significant effect.

DISCUSSION

Stimulation frequency, duration, and intensity influenced the central contribution to plantar flexion torque. To maximize the production of central torque, stimulation trains with frequencies ≥80 Hz and relatively low stimulation intensities should be used. Constant-frequency stimulation patterns should be at

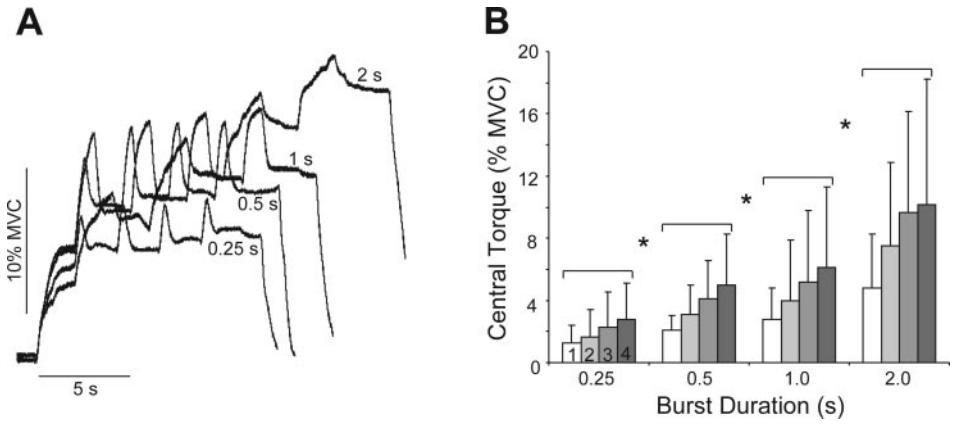

Fig. 4. Burst duration had a significant effect on ankle torque. *A*: sample data for single-burst patterns in 1 subject illustrating the development of central torque following bursts of various durations. *B*: number of bursts and burst duration each significantly influenced central torque. Columns within each burst duration (0.25, 0.5, 1.0, or 2.0 s) represent the central torque present following 1, 2, 3, and 4 bursts. *Significant difference between adjacent burst duration groups, $P < 0.05$.

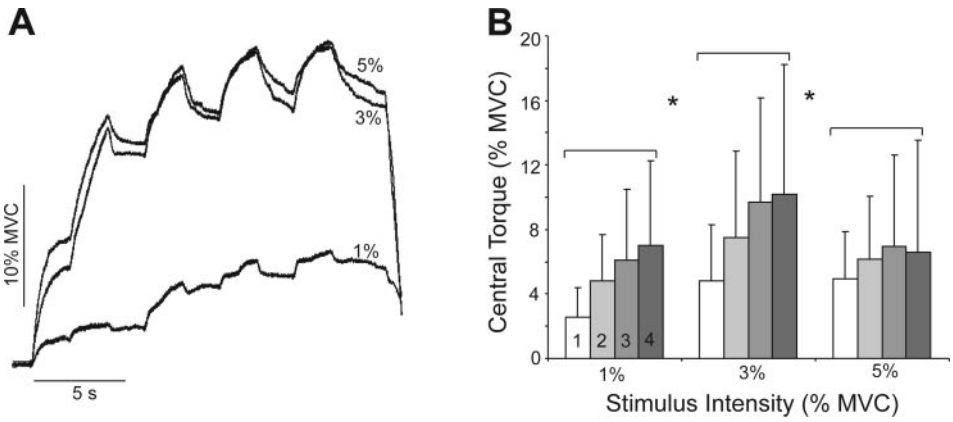

Fig. 5. Contraction intensity had a significant effect on ankle torque. *A*: sample data for single burst patterns in 1 subject illustrating the development of central torque following bursts at various stimulus intensities. *B*: number of bursts and the contraction intensity each significantly influenced central torque. The columns within each contraction intensity level (1, 3, or 5% MVC) represent the central torque present following 1, 2, 3, and 4 bursts. *Significant difference between adjacent stimulus intensity groups, $P < 0.05$.

least 11 s long, and burst patterns should have three repeated bursts of 2-s duration. These results are consistent with our hypothesis that increasing the afferent volley to the spinal cord (by increasing stimulation frequency or duration) would increase the central contribution to torque, whereas higher stimulation intensities would reduce central torque through antidromic block of motor axons.

The central contribution to torque scaled nonlinearly with stimulation frequency. A stimulation frequency above 20 Hz was required to activate the central mechanism, and higher frequencies were more effective in generating central torques. The results from the burst patterns indicate that there was a limit to the effectiveness of increasing stimulation frequency to generate more central torque. The central torque gradually increased with stimulation rate at the intermediate frequencies (40 and 60 Hz), but it leveled off at the higher frequencies (80 and 100 Hz). Above 80 Hz, increasing the number of pulses delivered in a certain time frame was not effective in activating additional motoneurons, possibly as a result of the sensory axon being unable to consistently follow the higher frequency stimulation.

Torque increased during constant-frequency stimulation, a finding consistent with the synaptic recruitment of additional motor units over time through either presynaptic or postsynaptic mechanisms. Earlier work indicates that this torque development is not due to a peripheral mechanism (7, 8). Posttetanic potentiation increases neurotransmitter release from sensory axons through repeated stimulation, potentially activating higher threshold motoneurons. Alternatively, the sensory volley could activate motoneuron plateau potentials. Individual neurons can develop plateau potentials at different levels of excitatory input (3). Therefore, the increase in torque may occur during the stimulation as plateau potentials develop at different times in individual neurons. However, the time course of central torque development was not consistent with reported values for the development of plateau potentials. In the constant-frequency trials, the magnitude of the central torque was still increasing after an average of over 10 s (range 3.2–16.6 s) of stimulation. In contrast, earlier studies have reported that plateau potentials develop with a time course of 4–6 s, implying that any torque increases due to plateau potentials should be complete within this time period (2, 15, 33). The longer time course reported in our results may indicate that plateau potentials are not solely responsible for the development of central torque. The magnitude of central torque may be a function of interplay between the development of PTP and PICs, because increased neurotransmitter release associated with PTP activates plateau potentials in additional spinal neurons.

We propose that the mechanism responsible for the gradually increasing torque during constant-frequency stimulation is also responsible for the increased torque following bursts of high-frequency stimulation. However, these two stimulation conditions differ in whether high-frequency (>20 Hz) afferent input is continuous or periodic. Lee and Heckman (28) have reported that PICs in some neurons (termed "fully bistable") produce steady self-sustained firing following brief excitatory inputs, whereas other neurons (termed "partially bistable") cease firing once the excitation is removed. Therefore, it is possible that the central torque developed with constant-frequency patterns is produced by both the firing of fully and partially bistable neurons, whereas the central torque that remains following high-frequency bursts or even after the cessation of stimulation is produced solely by fully bistable neurons. In addition, PTP could potentially have a larger effect during sustained high-frequency stimulation. However, the similarity between the central torque produced by a 100 Hz constant frequency train (10.7% MVC) and four 100-Hz, 2-s bursts (10.2%) may indicate that partially bistable neurons and PTP do not contribute significantly more to the measured central torque during the constant-frequency train.

Central torque increased as the burst duration increased from 0.25 s to 2 s. These results are consistent with a torque development time course of over 10 s, as reported above. It is likely that increasing the burst duration beyond 2 s would have led to larger central torques, up to the level generated with the 20-s, 100-Hz train. However, multiple short bursts were as effective as longer bursts in activating the central mechanism, because the central torque generated by four 2-s 100-Hz bursts (10.2% MVC) was not significantly different from the central torque generated by 20 s of 100-Hz constant-frequency stimulation (10.7% MVC). Long stimulation durations are recommended to develop central torque. When using FES, static muscle contractions for grasping or standing could be generated using long-duration stimulation trains, generating torque through a central mechanism and possibly reducing fatigue. However, during tasks involving repetitive movement (walking, etc.), muscle contractions rarely last as long as 2 s, so multiple short bursts may be a more effective alternative for activating the central mechanism.

The central contribution to torque did not scale linearly with contraction intensity. In the constant-frequency trials, contraction intensity (1% or 3% MVC) did not have a significant effect on the magnitude of the central torque. When using the burst patterns, central torque was maximized at an intermediate level (3% MVC). Although the afferent volley likely scaled with intensity, at the highest intensity orthodromic action potentials in motor axons could have been blocked by antidromic volleys. In H-reflex studies, the contribution of sensory axon activation to motor unit recruitment is reflected by H-reflex magnitude, which increases with contraction intensity and then decreases as a result of antidromic collision in the motor axon. Therefore, we would expect the central contribution to torque to be largest at a relatively low contraction intensity, at which the H-reflex amplitude would likely be maximized.

Along with earlier work (1, 7, 8, 25, 29), our results indicate that the development of torque through surface NMES is dependent on a central mechanism, in which the activation of sensory axons contributes to muscular contractions. This finding is consistent with earlier work examining the central effects of NMES. Electrical stimulation can increase muscular strength in nonstimulated muscles through cross-education (22), produce neural adaptations resulting in increased muscle activation (12), and cause central fatigue (5). These results demonstrate that activating muscle through electrical stimulation is not simply a peripheral process. We have proposed a central mechanism by which sensory feedback excites motoneurons at the level of the spinal cord, but our results do not exclude the possibility of a supraspinal contribution, as previously suggested (5, 12). In addition to effects at the level of the spinal cord, electrical stimulation can also produce changes in cortical excitability (26). Speculatively, repeated NMES may alter the strength of the central mechanism whether located in the spinal cord or a supraspinal region, an issue not addressed by this study.

Surface NMES is used not only in rehabilitation settings but also as a research tool to examine muscle properties. For example, repetitive electrical stimulation can be used to induce muscular fatigue, quantified by the decrease in output torque. However, the present results indicate that the torque production of a muscle group is dependent on a central mechanism, not solely muscle characteristics. The gradual development of central torque during NMES may lead to an underestimation of fatigue. If possible, future work should attempt to control for this. The central mechanism is less likely to be activated when narrower stimulation pulses are used (27, 31, 34), or it could be prevented from contributing to torque by applying a nerve block proximal to the stimulation site (7, 8). Electromyographic activity should also be measured when possible, because the central contribution to torque may be influenced by H-reflex amplitude, which can change over time (25).

Our method of calculating central torque may underestimate the actual contribution of the central mechanism. We classified torque generated in the first 2 s of stimulation as peripheral. However, it is possible that some of this torque is produced through a central mechanism. Previous work has shown that H reflexes are present within the first 2 s of 20-Hz stimulation (25), implying that sensory feedback is contributing to muscular activation through a central pathway. Therefore, it is possible that the actual central contribution to torque is larger than that presented in this study.

The high variability in central torque between subjects (0–20% MVC in our results, up to 40% MVC in Ref. 8) may be explained by the variation among individuals in the level of monoamines present in the spinal cord (monoamine tone). In animal studies, the prevalence of plateau potentials produced by PICs may depend on monoamine tone (18, 19). Motoneuron plateau potentials are less likely to develop with low levels of spinal monoamines. In addition, the presence of self-sustained motoneuron firing in humans can be affected by factors such as caffeine intake, which was not controlled in this study (35). Some of the variation may also be due to difference in the time course and magnitude of posttetanic potentiation between subjects.

Rehabilitation applications of electrical stimulation would be improved by electrical stimulation patterns that can consistently recruit fatigue resistant fibers before fatigable fibers. Previous work has attempted to minimize fatigue through various stimulation strategies, including gradually reducing the stimulation frequency (6), activating the catchlike property of muscle with pulse doublets (4), and potentiating the muscle with high-frequency trains (32). These manipulations attempted to reduce or overcome fatigue through purely peripheral mechanisms, by mimicking activation patterns used by the central nervous system or taking advantage of muscular properties. By activating motor units synaptically, in the natural recruitment order (fatigue resistant first), patterns of wide-pulse stimulation may provide an alternative strategy to reduce fatigue.

The practical applications of activating muscle through the central mechanism may be limited by the magnitude of the muscle contraction that can be generated. In a healthy population, some subjects do not generate any central torque in response to wide-pulse stimulation (1 of 8 subjects in the present study; see also Ref. 25), whereas others produce up to 40% of a maximal contraction (8). Central torque can develop after spinal cord injury (7, 29); however, the magnitude of the effect may be smaller than in able-bodied subjects, and it should be further investigated. Even if unable to produce near-maximal contractions, the central mechanism may be useful in preventing atrophy by activating fatigue-resistant fibers at a relatively low-stimulation intensity. Otherwise, preventing fatigue-resistant fibers from converting to fatigable fibers with traditional methods may require much higher stimulus intensities, possibly causing discomfort in patients with sensation. Although pain was not quantified in this study, no subjects reported discomfort in response to frequent questioning, possibly as a result of the low stimulation intensities used. In FES applications, most repetitive movements do not require maximal muscle contractions. Generating these submaximal contractions by activating fatigue-resistant instead of fatigable fibers may help to prevent fatigue and allow longer lasting movements. We only investigated the development of central torque in a single muscle group. Further work should examine whether a central mechanism is effective in other muscles used in FES, particularly the quadriceps femoris. For a central mechanism of generating torque to be useful in producing functional movements, a method for turning off the central torque is also required. Reciprocal inhibition is one possible strategy for reducing the torque produced by the central mechanism. Electrical stimulation of an antagonist nerve can eliminate sustained muscle activity, and it may be effective in

abolishing the central torque (10, 30). A combination of techniques for initiating and terminating the torque produced by a central mechanism will be required for generating functional movements.

GRANTS

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