Effect of a peripheral nerve block on torque produced by repetitive electrical stimulation

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1Human Neurophysiology Laboratory, Faculty of Physical Education and Recreation, Centre for Neuroscience, University of Alberta, Edmonton, Alberta, Canada; 2Prince of Wales Medical Research Institute and University of New South Wales, Sydney, Australia; 3School of Human Kinetics and Brain Research Centre, University of British Columbia, Vancouver, British Columbia, Canada

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Lagerquist O, Walsh LD, Blouin JS, Collins DF, Gandevia SC. Effect of a peripheral nerve block on torque produced by repetitive electrical stimulation. J Appl Physiol 107: 161–167, 2009. First published April 23, 2009; doi:10.1152/japplphysiol.91635.2008.—Neuromuscular electrical stimulation (NMES) generates contractions by activation of motor axons (peripheral mechanism), but the afferent volley also contributes by recruiting spinal motoneurons synaptically (central mechanism), which recruits motoneurons according to Henneman’s size principle. Thus, we hypothesized that contractions that develop due to a combination of peripheral and central mechanisms will fatigue less rapidly than when electrically evoked contractions are generated by the activation of motor axons alone. Plantar-flexion torque evoked by NMES over the triceps surae was compared in five able-bodied subjects before (Intact) and during (Blocked) a complete anesthetic block of the tibial and common peroneal nerves. In the Blocked condition, plantar-flexion torque could only develop from the direct activation of motor axons beneath the stimulating electrodes. NMES was delivered using three protocols: protocol A, constant 100 Hz for 30 s; protocol B, four 2-s bursts of 100 Hz alternating with 20-Hz stimulation; and protocol C, alternating 100 Hz bursts (1 s on, 1 s off) for 30 s. The percent change in evoked plantar flexion torque from the beginning to the end of the stimulation differed (P < 0.05) between Intact and Blocked conditions for all protocols (Intact: protocol A = +125%, B = +230%, C = +78%; Blocked: protocol A = −79%, B = −15%, C = −35%). These results corroborate previous evidence that NMES can evoke contractions via the recruitment of spinal motoneurons in addition to the direct recruitment of motor axons. We now show that NMES delivered for periods of up to 30 s generates plantar-flexion torque which decreases when only motor axons are recruited and increases when the central nervous system can contribute.

NEUROMUSCULAR ELECTRICAL STIMULATION (NMES) is a common rehabilitation tool for generating contractions in paralyzed muscles (23, 34, 40). While it is well known that contractions develop due to the stimulation of motor axons beneath the stimulating electrodes (23, 34, 40), the contribution made by the electrically evoked afferent volley through the recruitment of spinal motoneurons (for a review, see Ref. 9) is not as well understood. The present experiments were designed to compare torque evoked by NMES over the triceps surae before a nerve block, when the connections between the central nervous system and periphery were intact (Intact), to torque generated when only the activation of distal motor axons could contribute due to a complete anesthetic block of the tibial and common peroneal nerves (Blocked). The goal was to provide insight into how NMES generates contractions and to test the hypothesis that torque generated during the Intact condition will show less fatigue compared with the Blocked condition. Fatigue in humans has been defined as any exercise-induced decrease in maximal voluntary force produced by a muscle (17). For the present experiments, since we were not able to evaluate voluntary force during our Blocked condition and because our stimulus intensity was purposely not maximal, we will refer to fatigue as a decrease in submaximal electrically evoked tetanic force.

When NMES is delivered at high stimulus intensities, the large antidromic volley in motor axons ensures that the evoked contraction will be driven largely by the direct depolarization of motor axons beneath the stimulation site with little or no contribution from the central nervous system; however, when using lower stimulus intensities, long stimulus trains, and high frequencies the electrically evoked afferent volley recruits motoneurons synaptically, generating up to 40% of a maximal voluntary contraction (MVC) (9–11). Thus, NMES can evoke contractions from both the direct activation of motor axons (peripheral mechanism) and recruitment of spinal motoneurons (central mechanism) (1, 3, 9–12, 27, 35). This central contribution to the evoked contraction has been confirmed by applying NMES before and during a complete anesthetic block of the nerve proximal to the stimulation site (3, 10, 11). This showed that more torque developed during NMES before the nerve block, when the central nervous system could contribute, than during the nerve block when only the activation of motor axons could contribute, and highlights the importance of considering the central recruitment of motoneurons during NMES (39).

We have shown that the central contribution involves motor unit recruitment that is time locked to each stimulus pulse, reflecting transmission along the Hoffmann reflex (H-reflex) pathway (27), as well as motor unit discharge that is asynchronous with the stimulus pulses (10). The electrically evoked afferent volley elicited by low-intensity NMES has been hypothesized to recruit motor units with low voluntary recruitment thresholds (1, 3, 9–12, 27, 35) as predicted for synaptic recruitment based on Henneman’s size principle (2, 5, 21). These low-threshold motoneurons innervate muscle fibers that are the most fatigue resistant (6). As described by Henneman’s size principle, voluntary contractions initially recruit small, fatigue-resistant motor units as the intensity of the contraction increases (11). NMES, on the other hand, has been reported to
recruit motor units in a reversed (22, 43), random (15, 19, 24, 28), or near-normal order (42) compared with voluntary contractions. Whatever the exact recruitment order, it is generally agreed that the fatigue (i.e., decline in electrically evoked torque) observed during NMES is largely due to the direct recruitment of motor axons (peripheral mechanism) (19), which does not follow Henneman’s size principle. Thus, we hypothesized that electrically evoked contractions that develop due to a combination of peripheral and central mechanisms will fatigue less than contractions evoked solely via motor axon stimulation. In contrast to our previous experiments (1, 3, 9–12, 27, 35), we increased the length of the stimulus trains and decreased the pause between successive trains to evaluate the decrease in torque over time. By using stimulation patterns that incorporated both 20 Hz (a recommended frequency for NMES of the lower extremities; 40) and 100 Hz, we compared torque generated during a typical NMES frequency, as well as high-frequency stimulation that enhances the central contribution to the evoked contractions.

**METHODS**

Five male volunteers (28–53 yr old; 55–80 kg; 1.65–1.87 m) free from neurological and musculoskeletal disorders participated after providing informed, written consent. Since we were interested in quantifying torque generated by the combination of peripheral and central mechanisms, we only studied subjects who had previously displayed torque that increased during tetanic stimulation, as this is consistent with a central contribution to the evoked contraction (1, 3, 9–12, 27, 35). Central contributions typically occur in >85% of participants when high frequencies and wide pulse widths (1, 3, 9–12, 27, 35) are used. Experiments were conducted at the Prince of Wales Medical Research Institute in Sydney, Australia, and were approved by the University of New South Wales Human Research Ethics Committee. All experimental procedures were performed on the right leg while subjects were seated with straps to hold the foot and knee securely in place. Each subject participated in the Intact and Blocked conditions on the same day, beginning with the Intact condition. The order of protocols was randomized for each individual subject, and this order was maintained across Intact and Blocked conditions. To minimize any effect of fatigue between the Intact and Blocked condition, a minimum of 2 h separated the end of testing during the Intact condition and the beginning of data collection during the Blocked condition. In addition, supramaximal twitch data were not different between any pre- vs. post- or Intact vs. Blocked conditions (see Table 1), suggesting that our results were not influenced by fatigue. The right hip, knee, and ankle were positioned at ~90°, 90°, and 90 degrees, respectively. Torque was measured with an S-type fatigue. The right hip, knee, and ankle were positioned at different between any pre- vs. post- or Intact vs. Blocked conditions

|Table 1. Peak torque generated by supramaximal single and doublet stimuli delivered prior to (Pre) and after (Post) each stimulation protocol for the Intact and Blocked conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intact Pre</th>
<th>Intact Post</th>
<th>Blocked Pre</th>
<th>Blocked Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single</td>
<td>17.7±2.9</td>
<td>18.1±3.0</td>
<td>16.4±3.2</td>
<td>16.4±3.1</td>
</tr>
<tr>
<td>Doublet</td>
<td>30.1±5.6</td>
<td>30.8±5.7</td>
<td>29.3±5.5</td>
<td>29.7±5.6</td>
</tr>
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Group data in newton-meters; means ± SE.
nation. All participants were retested at the end of the experimental session to ensure that the block had not dissipated during the experiments (~3 h).

Analysis and statistics. Data were collected using Spike 2 software (Cambridge Electronic Design). To quantify torque, 60 torque-time integrals were calculated at equal time intervals for stimulation protocols A and B. For protocol C, 120 torque-time integrals were calculated. All torque-time integrals were calculated over a 0.5-s interval. Statistical analyses were performed on group data to compare differences in torque-time integrals at the beginning vs. the end of stimulation between Intact and Blocked conditions for each protocol. For protocols A and B, each subject’s second (Time 1) and 29th (Time 2) torque-time integrals (1.25–1.75 s) were averaged across the first and second stimulus trains (see Fig. 1, A and B). These values were then used to calculate the mean torque-time integrals at Time 1 and Time 2 for the group. For protocol C, each subject’s first (Time 1) and 15th (Time 2) torque time integrals were averaged across each stimulation train (n = 8; see Fig. 1C). These values were then used to calculate the mean torque-time integrals at Time 1 and Time 2 for the group. For each subject, the percent change in torque from the beginning to the end of the stimulation were significantly different (P < 0.05) between Intact and Blocked conditions for all three protocols (Intact protocol A = 125%, protocol B = 230%, protocol C = 78%; Blocked protocol A = −79%, protocol B = −15%, protocol C = −35%).

Protocol A: constant 100-Hz stimulation. Figure 2A shows data from a single subject in whom torque remained relatively constant throughout the 30 s of 100-Hz stimulation during the Intact condition. During Blocked condition, torque dropped from an initial value of 30% MVC to 10% MVC within 20 s. The group data (Fig. 2B) show a similar pattern, with mean torque-time integrals increasing 125% from the beginning to the end of the stimulation (Time 1 to Time 2) during the Intact condition. In contrast, there was a 79% decrease in the mean torque-time integrals as the participant moved to the Blocked condition.

RESULTS

During the Intact condition, torque increased on average 144% from Time 1 to Time 2 across all stimulation protocols. In contrast, in the Blocked condition, torque decreased on average 43% across all stimulation protocols. Torque percent change scores from the beginning to the end of the stimulation were significantly different (P < 0.05) between Intact and Blocked conditions for all three protocols (Intact protocol A = +125%, protocol B = +230%, protocol C = +78%; Blocked protocol A = −79%, protocol B = −15%, protocol C = −35%).

Cohen’s d effect sizes were calculated for changes between Time 1 vs. Time 2 for all protocols during both Intact and Blocked conditions. Effect size measures the magnitude of a treatment effect but, unlike significance tests, are independent of sample size. Cohen’s d is defined as the difference between the means, M1 − M2, divided by the pooled standard deviation, SD, (d = M1 − M2/SD). Effects sizes were defined as “small, d ≤ 0.2”, “medium, 0.2 ≤ d ≤ 0.8”, and “large, d ≥ 0.8” as described by Cohen (8).
torque-time integrals from *Time 1* to *Time 2* during the Blocked condition. The effect sizes for both the increase and decrease in torque during the stimulation were large (Intact $d = 1.0$; Blocked $d = 1.3$) and the percent change scores between torque-time integrals for the Intact and Blocked conditions were significantly different ($P < 0.05$). The mean torque-time integrals at *Time 1* were not significantly different between Intact and Blocked trials, indicating torque at the beginning of the stimulation was similar between conditions.

**Protocol B:** four 2-s “bursts” of 100 Hz alternating with 20 Hz stimulation.Figure 3 shows data from a single subject in whom torque increased from an initial value of $5\%$ MVC to eventually reach $15\%$ MVC after four bursts of 100-Hz stimulation during the Intact condition. This increase in torque
did not occur during the Blocked condition. This stimulation protocol resulted in a 230% increase in the mean torque-time integral from Time 1 to Time 2 across the group (Fig. 3B) during the Intact condition. In contrast, the mean average torque-time integral decreased 15% during the Blocked condition. The effect sizes for the increase and decrease in torque during the stimulation were large and small, respectively (Intact $d = 1.1$; Blocked $d = 0.24$). These percent changes for the Intact and Blocked conditions were significantly different ($P < 0.05$). The mean torque-time integrals at Time 1 were not significantly different in the Intact vs. Blocked protocol, thus torque at the beginning of the stimulation was similar between conditions.

**Protocol C: alternating on-off 100-Hz stimulation.** The data from one subject during stimulation with protocol C are shown in Fig. 4A. For this subject, torque increased $\sim 10\%$ MVC from the first to the last train of stimulation during the Intact condition, whereas it decreased by $\sim 2\%$ MVC during the Blocked condition. On average for the group, torque-time integrals increased 78% (medium effect, $d = 0.41$) and decreased 35% (medium effect, $d = 0.48$) in the Intact and Blocked conditions, respectively. These percent changes between the Intact and Blocked conditions were significantly different ($P < 0.05$). The mean torque-time integrals at Time 1 were significantly different ($P < 0.05$) during the Intact vs. Blocked protocol. Thus, there was significantly more torque at Time 1 for the Blocked vs. the Intact condition.

**Supramaximal single and doublet stimulation.** Peak torque evoked during the supramaximal single and doublet stimulation was not significantly different before vs. after NMES for any protocol (A, B, and C; see Table 1).

**Sustained plantar-flexion torque.** During the Intact condition four of the five subjects regularly had sustained plantar-flexion torque that outlasted the electrical stimulation. Examples are shown in Figs. 3A and 4A, indicated by the arrow labeled “end of stimulation.” This sustained activity was never present during the Blocked condition for any subject.

**DISCUSSION**

In the Intact condition, torque increased during all stimulation protocols on average by 144% from Time 1 to Time 2. In contrast, during the Blocked condition, torque decreased on average by 43% from Time 1 to Time 2 across all protocols. Thus, results support the hypothesis that electrically evoked contractions, which develop due to a combination of peripheral and central mechanisms, fatigue less than contractions evoked solely due to motor axon stimulation. The use of high stimulation frequencies increases the rate of afferent volleys reaching motoneurons, while wide stimulus pulse widths increase the likelihood of activating sensory axons (14, 29, 30, 45).

During a voluntary contraction, motor unit recruitment usually begins with small, fatigue-resistant units and proceeds through the larger, more fatiguable units as the contraction increases, as described by Henneman’s “size principle” (21). It is generally accepted that NMES recruits motor units in a different order compared with voluntary contractions; however, whether motor units are recruited in a reversed (22, 43), random (15, 19, 24, 28), or near-normal order (41) compared with voluntary contractions is controversial. Despite evidence to the contrary (1, 3, 9–12, 27, 35), descriptions of how contractions are generated by NMES are generally limited to...
the depolarization of motor axons (23, 34, 40) and the possibility of a central contribution is often not considered (7, 13, 23, 34, 40). A recent editorial has highlighted the importance of considering a central recruitment of motoneurons during NMES and that such activation has potential therapeutic advantages (39). If NMES does not involve the synaptic recruitment of motoneurons, we would not have observed any difference between torques produced in Intact vs. Blocked conditions in the present study. On the contrary, torque decreased in Blocked conditions and increased during Intact conditions. Our results suggest that in the intact state, NMES generates contractions from both the direct depolarization of motor axons and the central recruitment of low-threshold, fatigue-resistant motor units.

Torque generated from a central recruitment of motoneurons during NMES is prominent when using high frequencies and wide pulse widths (1, 3, 9–12, 27, 35) that maximize the afferent volley (14). Low stimulus intensities are especially effective at generating torque from a central recruitment of motoneurons, presumably due to a decreased probability of antidromic block along motor axons (12). Thus, recruitment of motor units exclusively by the direct depolarization of motor axons is likely to occur only at high stimulus intensities, when the antidromic volley will block orthodromic propagation along motor axons. As the intensity of stimulation in the present study evoked an initial contraction of 5–10% MVC during 2 s of 20-Hz stimulation, we expect there was minimal antidromic collision along motor axons, thus allowing synaptically-activated motoneurons to evoke torque in part from the recruitment of small, fatigue-resistant motor units. Both protocols A and B showed well-matched torques at the beginning of stimulation between Intact and Blocked trials; but since we could not match torque at Time 1 during protocol C it is possible that for this protocol, subjects fatigued more during the Blocked condition due to the higher starting torque relative to the Intact condition.

The increase in NMES-generated torque during the Intact condition reflects the additional synaptic recruitment of motoneurons. Our working hypothesis is that the afferent volley generated during NMES recruits according to Henneman’s size principle; thus recruiting the low-threshold, fatigue-resistant motoneurons first. This central contribution to the evoked torque may be due to a synchronous reflex action and/or motoneuron discharge that is synchronous with the stimulus pulses. In contrast, contractions evoked during the blocked condition likely involve the synchronous activation of a greater proportion of fast-fatigable motor units (15, 19, 22, 24, 28, 43), thus resulting in the decline in torque that we observed. The electrically evoked afferent volley during NMES can generate an H-reflex and hence the synchronous, reflexive activation of motoneurons. Reflex activation of motoneurons is not traditionally believed to contribute to force generation during NMES because the H-reflex is attenuated as stimulus rates above 0.1 Hz due to postactivation depression (37). However, the H-reflex can recover following this initial depression (27, 36) and may contribute to force generation during NMES in some muscles (9, 27). Another possibility is that the afferent volley generated during NMES results in the asynchronous discharge of motoneurons due to the activation of persistent inward currents in spinal neurons. Such currents can cause repetitive firing in the absence of synaptic input and are most prominent in low-threshold, fatigue-resistant motoneurons (20, 31, 32). Electrical stimulation (10, 11, 36) and vibration (18, 25) can cause self-sustained firing in motoneurons, resulting in contractions that outlast the stimulation and are thought to be sustained by persistent inward currents (see End of stimulation Fig. 3A and 4A). During the present experiments, four out of the five subjects produced plantar-flexion torque that outlasted the stimulation in the Intact condition only. No one produced torque that outlasted the stimulation during the Blocked condition. These results show that sustained plantar-flexion torque depends on a central mechanism but does not differentiate between a spinal or cortical origin.

Another mechanism that could contribute to the increasing torque in the Intact condition is the progressive recruitment of more motor axons during the stimulation. There is evidence that persistent inward Na⁺ currents can develop in motor axons (42), which could explain a progressive depolarization and thus recruitment of motor axons; however, an increased recruitment of motor axons is not consistent with the significant difference in torque that we observed between the Intact and Blocked conditions. If the elevated torque during the Intact condition were due to increased motor axon recruitment, we would expect the same results during the Blocked condition since the ability to activate motor axons directly is not affected by the nerve block. In addition, the repetitive activation hyperpolarizes motor axons and thus decreases the likelihood of recruitment (26, 44). It is therefore most likely that the increased torque during the Intact protocols was due to the progressive, central recruitment of motoneurons. The central recruitment of motoneurons by large-diameter afferent input is known to follow Henneman’s size principle (2, 5, 21), thus first recruiting motoneurons that innervate fatigue-resistant muscle fibers (20, 31, 32). The decreased torque during tetanic stimulation in the Blocked condition is likely due to the recruitment of relatively fewer motor units that are fatigue-resistant and an increase in motor axon threshold causing a loss of motor unit activation. While these mechanisms likely also contributed to a decline in torque during the Intact condition, this was offset by the central recruitment of motoneurons. Our results do not suggest the presence of a decline in force-generating capacity within the muscle since supramaximal single and doublet stimulation collected 2 s following NMES were not different from those evoked before the stimulation.

Conclusion. In the intact nervous system, NMES can generate contractions via the recruitment of spinal motoneurons in addition to the direct depolarization of motor axons. The present data suggest that recruiting motor units via synaptic drive vs. direct motor axon depolarization improves fatigue resistance during NMES compared with contractions that develop from the recruitment of motor axons alone. Recruiting fatigue-resistant motor units via central mechanisms that are less accessible via direct motor axon depolarization may slow muscle atrophy and the transformation from slow- to fast-twitch fiber types that occurs following spinal cord injury (4, 33). In addition, maximizing the activation of spinal motoneurons during NMES may have benefits for rehabilitation as it improves the resistance to electrically evoked muscle fatigue.

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REFERENCES


