

# The pulse duration of electrical stimulation influences H-reflexes but not corticospinal excitability for tibialis anterior

Alyssa R. Hindle, Jenny W.H. Lou, and David F. Collins

**Abstract:** The afferent volley generated by neuromuscular electrical stimulation (NMES) influences corticospinal (CS) excitability and frequent NMES sessions can strengthen CS pathways, resulting in long-term improvements in function. This afferent volley can be altered by manipulating NMES parameters. Presently, we manipulated one such parameter, pulse duration, during NMES over the common peroneal nerve and assessed the influence on H-reflexes and CS excitability. We hypothesized that compared with shorter pulse durations, longer pulses would (i) shift the H-reflex recruitment curve to the left, relative to the M-wave curve; and (ii) increase CS excitability more. Using 3 pulse durations (50, 200, 1000  $\mu$ s), M-wave and H-reflex recruitment curves were collected and, in separate experiments, CS excitability was assessed by comparing motor evoked potentials elicited before and after 30 min of NMES. Despite finding a leftward shift in the H-reflex recruitment curve when using the 1000  $\mu$ s pulse duration, consistent with a larger afferent volley for a given efferent volley, the increases in CS excitability were not influenced by pulse duration. Hence, although manipulating pulse duration can alter the relative recruitment of afferents and efferents in the common peroneal nerve, under the present experimental conditions it is ineffective for maximizing CS excitability for rehabilitation.

**Key words:** neuromuscular electrical stimulation, rehabilitation, neuroplasticity, corticospinal excitability, H-reflex.

**Résumé :** La volée afférente générée par une stimulation neuromusculaire électrique (SNME) influence l'excitabilité cortico-spinale (CS) et de fréquentes sessions de SNME peuvent renforcer les voies CS, résultant en des améliorations fonctionnelles à long terme. Cette volée afférente peut être modifiée par la manipulation des paramètres de la SNME. Dans l'étude présente, les auteurs ont manipulé un de ces paramètres, la durée de l'impulsion, lors d'une SNME appliquée sur le nerf péronier commun, et ils en ont évalué l'effet sur le réflexe H et l'excitabilité CS. Ils ont posé l'hypothèse que, comparativement à des impulsions de plus courtes durées, des impulsions plus longues pourraient (i) déplacer la courbe de recrutement du réflexe H vers la gauche relativement à la courbe de l'onde M et (ii) augmenter davantage l'excitabilité CS. En utilisant trois durées d'impulsion (50, 200 et 1000  $\mu$ s), les courbes de recrutement de l'onde M et du réflexe H ont été recueillies et, lors d'expériences séparées, l'excitabilité CS a été évaluée en comparant les potentiels moteurs évoqués déclenchés avant et après 30 minutes de SNME. Malgré un déplacement vers la gauche de la courbe de recrutement du réflexe H lors de l'utilisation d'une impulsion de 1000  $\mu$ s, conformément à une volée afférente plus importante pour une volée efférente donnée, les augmentations d'excitabilité CS n'étaient pas influencées par la durée de l'impulsion. Ainsi, même si la manipulation de la durée de l'impulsion peut modifier le recrutement relatif des afférents et des efférents du nerf péronier commun, les conditions expérimentales présentes constituent une stratégie inefficace pour maximiser l'excitabilité CS en réadaptation. [Traduit par la Rédaction]

**Mots-clés :** stimulation neuromusculaire électrique, réadaptation, neuroplasticité, excitabilité cortico-spinale, réflexe H.

## Introduction

Neuromuscular electrical stimulation (NMES) involves the repetitive application of pulses of stimulation over a muscle belly or nerve trunk and can restore movement and reduce muscle atrophy for people who have had a spinal cord injury or stroke (Sheffler and Chae 2007; Bergquist et al. 2011). NMES activates both efferent and afferent axons, resulting in muscle contractions and the transmission of an afferent volley to the central nervous system, respectively. At the level of the brain, the afferent volley evoked by a single session of NMES can increase the excitability of the motor cortex (Ridding et al. 2000; Kaelin-Lang et al. 2002; Khaslavskaja et al. 2002). After repeated NMES sessions, this effect can “strengthen” corticospinal (CS) pathways, as reflected by prolonged increases in the amplitudes of motor evoked potentials (MEPs) (McKay et al. 2002; Everaert et al. 2010) and lasting improvements in movement (Liberson et al. 1961; Fraser et al. 2002; Stein

et al. 2010). To capitalize on this effect for rehabilitation, it is important to understand how to maximize the influence of NMES on CS excitability. One way to do this is to optimize the parameters of NMES, which include pulse amplitude, frequency, and duration, to increase the electrically evoked afferent volley and the effect that NMES has on CS excitability (Mang et al. 2010; Chipchase et al. 2011). Currently, the effect of each NMES parameter on CS excitability is not well defined. However, there is evidence that increasing NMES pulse amplitude (Chipchase et al. 2011) and frequency (Mang et al. 2010) increases CS excitability. The main goal of the present study was to investigate the effect of the third parameter, NMES pulse duration, on CS excitability. We studied the common peroneal (CP) nerve because it is often stimulated to reduce “foot-drop” (Liberson et al. 1961; Everaert et al. 2010) and, while a single session of NMES over the CP nerve increases CS excitability in the short-term (Khaslavskaja et al. 2002;

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Mang et al. 2010; Thompson et al. 2011), frequent CP nerve stimulation can strengthen CS pathways to tibialis anterior (TA) (Liberson et al. 1961; Everaert et al. 2010), resulting in long-term improvements in function even when the stimulation is off (Liberson et al. 1961; Stein et al. 2010).

Relatively long pulse durations preferentially recruit afferent axons over efferent axons in the tibial (Lin et al. 2002; Lagerquist and Collins 2008), ulnar (Bostock and Rothwell 1997), median, and radial nerves (Panizza et al. 1998). This preferential recruitment of afferent axons with longer pulse durations is due to the lower rheobase and longer strength-duration time constant ( $\tau_{SD}$ ) of afferent versus efferent axons (Veale et al. 1973; Burke et al. 2001). Whether long pulse durations also preferentially recruit afferents in the CP nerve has not been evaluated and thus the first goal of the present study was to identify whether increasing pulse duration increases the electrically evoked afferent volley, relative to the efferent volley, in the CP nerve. Data were collected to construct M-wave and H-reflex recruitment curves (MH-RCs) for TA using 3 pulse durations (50, 200, 1000  $\mu$ s). We hypothesized that there would be a leftward shift in the H-reflex recruitment curve (an indirect measure of the afferent volley) relative to the M-wave curve (an indirect measure of the efferent volley) with longer pulse durations, consistent with the recruitment of more afferent axons relative to efferent axons with longer pulses (Panizza et al. 1989; Lagerquist and Collins 2008). Thus, we predicted that the current required to generate maximal H-reflexes ( $H_{max}$ ), expressed as a percentage of the current required to generate the maximal M-wave ( $M_{max}$ ), would be significantly less for the longer pulses. We also predicted that  $H_{max}$  would be larger when using the long, compared with short, pulses. These experiments confirmed that longer pulse durations preferentially recruit afferent fibres in the CP nerve. Accordingly, we went on to test our main hypothesis that the relatively large afferent volley generated when using long pulse durations would increase CS excitability more than when shorter pulses were used. NMES was delivered intermittently (20 s "on", 20 s "off") for 30 min at each of the 3 pulse durations on separate days. CS excitability was assessed by comparing the amplitudes of MEPs generated before and after each NMES session. NMES was delivered to generate equivalent M-waves with each pulse duration, thus we predicted that MEPs would increase more after the NMES sessions that incorporated the longer pulses, consistent with a larger afferent volley reaching the cortex. Together, these experiments are part of a larger body of work designed to identify NMES parameters that maximize the beneficial effects on circuits in the central nervous system for rehabilitation (Bergquist et al. 2011; Chipchase et al. 2011).

## Materials and methods

Nine men and 11 women ranging in age from 18 to 50 years with no known neurological disorders participated in this study. The procedures were approved by the Research Ethics Board at the University of Alberta, and all subjects gave written informed consent prior to testing. For participants who had not previously experienced either NMES or transcranial magnetic stimulation (TMS), a brief orientation session was completed several days prior to the data collection sessions. For all sessions, the participants were seated in a Biodex dynamometer chair (System 3, Biodex Medical Systems, Shirley, N.Y., USA) with the right knee at 100° and the ankle at 90°, and their right foot secured to a footplate. The stimulation was delivered using a constant current stimulator (Digitimer DS7A or DS7AH, Welwyn Garden City, UK). Participants were instructed to avoid caffeine for 12 h prior to the experiment, and to avoid strenuous exercise for 6 h prior.

## Electromyography (EMG)

EMG was recorded from TA of the right leg using disposable bipolar (2.25 cm<sup>2</sup>) surface recording electrodes (Vermed Medical, Vermont, USA) positioned approximately 1 cm apart. The ground

electrode was placed over the patella, or over the tibia, depending on whichever configuration elicited the least amount of noise in the EMG signal. The skin over TA was cleaned with alcohol and allowed to dry before applying the electrodes over the muscle belly. EMG signals were amplified (500 $\times$ ) and band-pass filtered (10–1000 Hz; NeuroLog System; Digitimer, Hertfordshire, England). Data collected to construct the MH-RCs were sampled at 50 000 Hz to provide sufficient resolution to accurately quantify stimulation current for the short pulse durations. For these trials, current was measured using a current probe (mA 2000 Noncontact Milliammeter; Bell Technologies, Orlando, Fla., USA). Data collected during the sessions designed to assess changes in CS excitability were sampled at 5000 Hz.

## M-wave and H-reflex recruitment curves

All 20 participants completed a single ~30-min session in which data were collected to construct MH-RCs at each of the 3 pulse durations (50, 200, 1000  $\mu$ s). The order of testing each pulse duration was randomized between the participants. For each MH-RC, 40 pulses of stimulation were delivered over the CP nerve, with 8–10 s between pulses. The NMES was applied using round (3.2 cm diameter) neurostimulation electrodes (Axelgaard Manufacturing Co., Ltd.) arranged in a bipolar configuration, with the cathode proximal. Stimulation electrodes were placed posterior and distal to the head of the fibula, separated by approximately 1 cm. The stimulation amplitude was varied randomly from below M-wave and H-reflex thresholds to ~1.1 $\times$  the current required to generate  $M_{max}$ . Prior to collecting data for the MH-RCs, subjects performed 3 maximum voluntary dorsiflexion contractions (MVCs) while receiving verbal encouragement to perform maximally. Fourteen of these 20 participants also performed MVCs after the data were collected for the recruitment curves. During data collection, subjects held a TA contraction, equivalent to ~5% of the peak EMG recorded during the largest of the 3 MVCs performed prior to data collection, using visual feedback of the rectified and low-pass filtered (0.3 Hz) EMG signal. Subjects were instructed to relax between pulses of stimulation and were prompted to resume their contraction approximately 2 s prior to each stimulation pulse.

## Corticospinal excitability

Fifteen of the 20 participants took part in the experiments designed to evaluate the effect of pulse duration on CS excitability. These participants completed three ~2-h sessions, at least 48 h apart, in which NMES was applied at each of the 3 pulse durations (50, 200, 1000  $\mu$ s) in different sessions. The order of the different sessions was randomized between participants. For a given participant, these sessions were held at the same time of day to control for diurnal changes in CS excitability (Tamm et al. 2009). All participants performed MVCs (as described above) before and after the NMES session. CS excitability was measured before and after the NMES. NMES was delivered for 30 min (100 Hz, 20 s-on-20 s off) over the CP nerve to evoke an M-wave in TA that was 10%–15%  $M_{max}$ .

$M_{max}$  was used to monitor EMG recording site consistency; if the amplitude of  $M_{max}$  changed more than 20%, the site was cleaned with alcohol, allowed to dry, and the electrodes were replaced. Three  $M_{max}$  measurements were collected before and after the NMES. Additionally, after 15 min of NMES, the stimulation was paused to collect 3  $M_{max}$  measures. At this time, if necessary, current amplitude was adjusted to maintain an M-wave of 10%–15%  $M_{max}$ .

To assess CS excitability, TMS (Magpro R30; Medtronic Inc., Minneapolis, Minn., USA) was applied with a figure-of-eight coil (Medtronic MC-B70, Medtronic Inc.) to generate MEPs in TA. The TMS coil was positioned at a 45° angle relative to the predicted orientation of the central sulcus with the handle pointing backwards. All MEPs were generated while the subject was at rest. The "hotspot" for TA was identified by locating the position over the scalp where, at a constant TMS intensity, the largest MEP was

generated from TA. This location was recorded using a Brainsight image-guided stimulation system (Rogue Research, Montreal, Que., Canada). CS excitability measures consisted of 20 MEPs collected immediately before and after the NMES session. The stimulation was delivered over the TA hotspot at 1.2× resting MEP threshold (RMT), with 6–8 s between pulses. RMT was determined *before* the 30 min of NMES; thus, for a given participant, the TMS intensity as a percent of stimulator output was the same pre- and post-NMES. RMT was defined as the lowest TMS intensity that elicited an MEP amplitude of at least ~50  $\mu\text{V}$  in at least 4 of 8 consecutive trials.

### Data analyses

All analyses were conducted on group data, and descriptive statistics are reported as mean  $\pm$  standard error. Statistical significance was set at  $p < 0.05$ .

### M-wave and H-reflex recruitment curves

MH-RC data from individual participants were included for analysis only if measurable H-reflexes were consistently evident in the EMG signal. Thus, data were included for analysis only if the average peak-to-peak amplitude in the EMG 30–45 ms after the stimulus artifact for the 20 sweeps of lowest current from each of the 3 MH-RCs was greater than 4.5%  $M_{\text{max}}$ . Based on this criterion, data from 12 participants were included in the MH-RC analyses. Additionally, to exclude the potential of including F-waves in the assessment of  $H_{\text{max}}$ , sweeps of data were excluded from the analyses in which the current was above that which evoked an H-reflex that was on the descending limb of the H-reflex recruitment curve. This cut-off ranged from 80% to 95% of the current required to generate  $M_{\text{max}}$ .

Two outcome measures were analyzed for each MH-RC:

1.  $i_{H_{\text{max}}}$ : the average current that evoked the 3 largest H-reflexes expressed as a percentage of the current that evoked the single largest M-wave.
2.  $H_{\text{max}}$  amplitude: the average amplitude of the 3 largest H-reflexes.

For both of these outcome measures, separate 1-way repeated measures ANOVAs (RM-ANOVAs) were run with 3 levels of pulse duration (50, 200, 1000  $\mu\text{s}$ ). When the RM-ANOVA analysis identified a significant difference, Tukey's Honestly Significant Different post hoc tests were run. Eight of the 12 participants whose data were used in these analyses of the MH-RCs performed MVCs before and after the recruitment curve data were collected. A paired  $t$  test was used to test for differences in the MVCs performed before and after data were collected for the MH-RCs across these 8 individuals.

### Corticospinal excitability

Changes in CS excitability were assessed by comparing the mean amplitudes of the MEPs collected before and after the NMES sessions across the group. MEPs were measured peak-to-peak and normalized to the  $M_{\text{max}}$  obtained closest in time. To ensure that inadvertent background muscle contractions did not influence MEP amplitudes, MEPs were removed from the analysis if there was EMG activity greater than 2 standard deviations from baseline in the 1 s prior to each MEP. "Baseline" was defined as the EMG activity in the 1 s prior to the first sweep in the file. Of the 1800 MEPs recorded from the participants (120 MEPs per participant), 9 were removed based on this criterion, which represents 0.5% of the total MEPs.

A 2-way RM-ANOVA test was used to test for differences in  $M_{\text{max}}$  amplitudes with time (3 levels: pre-, mid-, and post-NMES) and pulse duration (3 levels: 50, 200, 1000  $\mu\text{s}$ ) as factors. Separate RM-ANOVAs were also used to test for differences in MEP amplitudes and MVC amplitudes with time (2 levels: pre-, post-NMES) and pulse duration (3 levels: 50, 200, 1000  $\mu\text{s}$ ) as factors.

## Results

### M-wave and H-reflex recruitment curves

Data from MH-RCs collected using 50  $\mu\text{s}$  and 1000  $\mu\text{s}$  pulse durations for a single participant are shown in Fig. 1a. The left side of the panel shows mean ( $n = 3$ ) EMG waveforms depicting  $H_{\text{max}}$  for this individual. The large M-wave associated with  $H_{\text{max}}$  when using the 50  $\mu\text{s}$ , but not the 1000  $\mu\text{s}$ , pulse durations is consistent with a leftward shift in the H-reflex curve, relative to the M-wave curve, when using 1000  $\mu\text{s}$  pulses. This leftward shift in the H-reflex curve is represented in the data shown in right side of the panel by the lower current, expressed as a percent of the current that produced  $M_{\text{max}}$ , which was required to evoke  $H_{\text{max}}$  with the longer pulse duration. The amplitude of  $H_{\text{max}}$  was similar for both pulse durations in this individual.

Across the group of participants, the current required to produce  $H_{\text{max}}$  (i.e.,  $i_{H_{\text{max}}}$ ), expressed as a percentage of the current required to produce  $M_{\text{max}}$ , was influenced by pulse duration; there was a main effect of pulse duration ( $F_{[2,22]} = 14.92, p = 0.0008$ ). Figure 2 shows  $i_{H_{\text{max}}}$  by pulse duration for each participant and for group mean data. The  $i_{H_{\text{max}}}$  was significantly smaller for 1000  $\mu\text{s}$  pulse durations than 50  $\mu\text{s}$  ( $p < 0.001$ ) and 200  $\mu\text{s}$  ( $p = 0.001$ ) durations. Across the 12 participants,  $i_{H_{\text{max}}}$  was 15%  $\pm$  4% smaller when generated with a 1000  $\mu\text{s}$  pulse duration than a 50  $\mu\text{s}$  pulse duration, and 13%  $\pm$  3% smaller when generated with a 1000  $\mu\text{s}$  pulse duration than a 200  $\mu\text{s}$  pulse duration.

There were no differences in  $H_{\text{max}}$  amplitudes between pulse durations, as there was no main effect of pulse duration ( $F_{[2,22]} = 1.312, p = 0.29$ ). When collapsed across pulse durations, the average  $H_{\text{max}}$  was 10.9%  $\pm$  0.4%  $M_{\text{max}}$ . There were also no differences in the amplitudes of MVCs performed before (21.5  $\pm$  2.7 Nm) and after (20.3  $\pm$  2.7 Nm) the data were collected for the MH-RCs ( $p > 0.05$ ).

### Corticospinal excitability

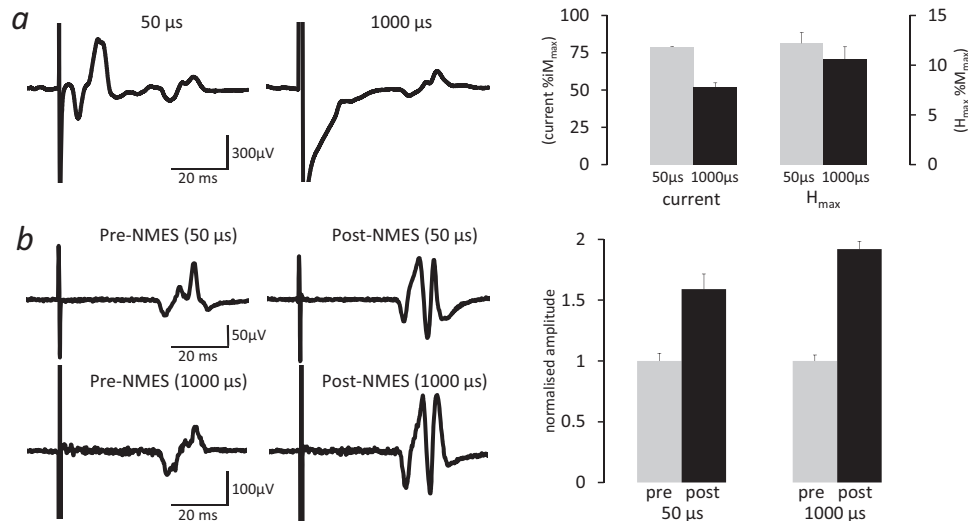
Figure 1b shows data collected before and after 30 min of NMES was delivered using 50 and 1000  $\mu\text{s}$  pulse durations; these data are from the same participant as in Fig. 1a. MEP amplitudes increased after NMES was delivered using both pulse durations. Although the magnitude of increase appears to be somewhat greater when using the 1000  $\mu\text{s}$  pulse duration, statistics were not performed on data from individual participants and this effect was not significant across the group (see below).

Across the group of 15 participants,  $M_{\text{max}}$  was not different between pulse durations and did not change over time for any pulse duration studied herein. For  $M_{\text{max}}$  there was no main effect of pulse duration ( $F_{[2,28]} = 0.752, p = 0.467$ ), no main effect of time ( $F_{[2,28]} = 1.695, p = 0.202$ ), and no interaction between pulse duration and time ( $F_{[4,56]} = 1.165, p = 0.336$ ). Collapsed across time, the group averages of  $M_{\text{max}}$  for pulse durations of 50  $\mu\text{s}$ , 200  $\mu\text{s}$ , and 1000  $\mu\text{s}$  were 6.6  $\pm$  1.1 mV, 5.5  $\pm$  0.6 mV, and 7.1  $\pm$  1.1 mV, respectively. Similarly, MVCs performed before and after the NMES sessions were not different. There was no significant main effect of time ( $F_{[1,14]} = 0.008, p = 0.928$ ) and no significant interaction ( $F_{[2,28]} = 0.044, p = 0.957$ ). When collapsed across all 3 pulse durations, MVCs before NMES were 21.3  $\pm$  2.3 Nm and after NMES were 21.3  $\pm$  2.2 Nm.

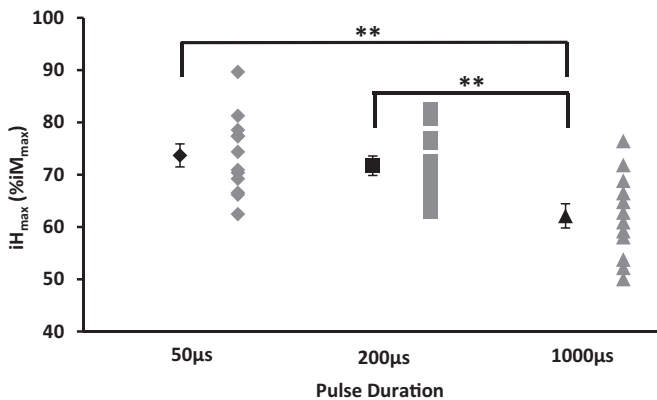
MEPs evoked at 1.2× RMT increased significantly following NMES, but this increase did not depend on pulse duration. There was a main effect of time ( $F_{[1,14]} = 7.29, p = 0.017$ ), no main effect of pulse duration ( $F_{[2,28]} = 1.169, p = 0.326$ ) and no interaction between pulse duration and time ( $F_{[2,28]} = 2.19, p = 0.131$ ). Fig. 3a shows mean MEP amplitudes for each participant and pulse duration pre- and post-NMES. Although variable in magnitude and even direction, CS excitability increased from pre- to post-NMES with each pulse duration for the majority of participants. Fig. 3b shows mean increases for the group for each pulse duration on the left, and the main effect of time on the right. The main effect of time shows that when collapsed across pulse durations, MEPs increased significantly and on average this increase was 52%  $\pm$  12%.



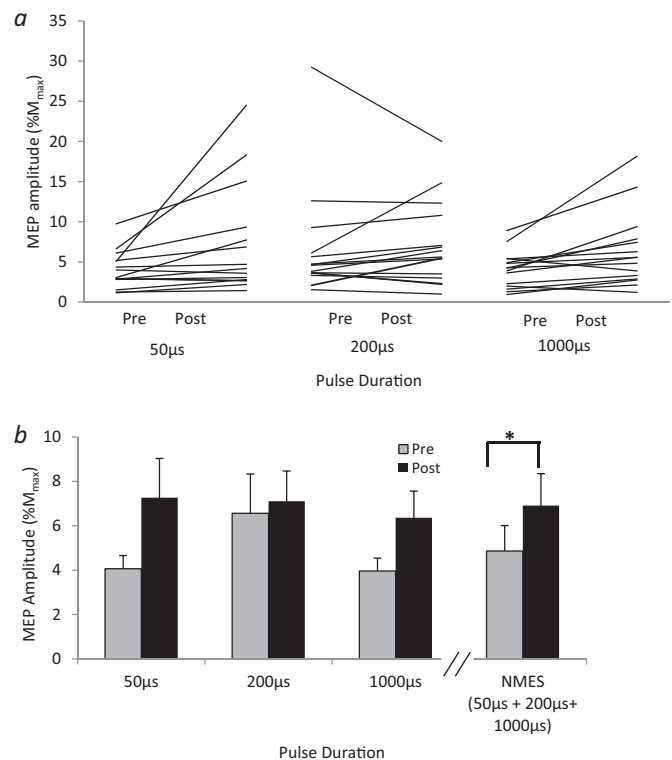
**Fig. 1.** Data collected from a single participant using 50 and 1000  $\mu\text{s}$  pulse durations. The left side of panel *a* shows electromyography waveforms that depict the mean of the 3 largest H-reflexes for this individual (i.e.,  $H_{\text{max}}$ ). The right side of panel *a* shows, for both pulse durations, the mean amplitude of  $H_{\text{max}}$  and the mean current, expressed as a percent of the current that evoked  $M_{\text{max}}$ , that evoked  $H_{\text{max}}$  for this individual. (*b*) The mean motor evoked potential (MEP) waveforms ( $n = 20$ ) and mean MEP amplitudes (normalized to the pre-MEP amplitude) collected before and after neuromuscular electrical stimulation (NMES) were delivered using the 2 pulse durations. (error bars = 1 SE)



**Fig. 2.** Current required to generate  $H_{\text{max}}$  expressed as a percentage of the current required to generate  $M_{\text{max}}$  (i.e.,  $i_{H_{\text{max}}}$ ). Shaded grey icons are data from each individual, and solid black icons show data averaged across the group ( $n = 12$ ; error bars = 1 SE; \*\*,  $p < 0.01$ ).



**Fig. 3.** Motor evoked potential (MEP) amplitudes from tibialis anterior pre- and post-NMES delivered with 50  $\mu\text{s}$ , 200  $\mu\text{s}$ , and 1000  $\mu\text{s}$  pulse durations. (*a*) Individual responses and (*b*) data averaged across the group ( $n = 15$ ; error bars = 1 SE; \*,  $p < 0.05$ ). NMES, neuromuscular electrical stimulation.



## Discussion

NMES rehabilitation can result in improvements in function that outlast the stimulation (Liberson et al. 1961; Everaert et al. 2010) and these are attributed to increased CS excitability associated with the electrically evoked afferent volley (Fraser et al. 2002; Everaert et al. 2010). Accordingly, it is important to identify which parameters of NMES best increase CS excitability. Given that increasing the electrically evoked afferent volley by manipulating pulse amplitude (Chipchase et al. 2011) and frequency (Mang et al. 2010) increases CS excitability, we predicted that longer pulse durations would also enhance the afferent volley and increase CS excitability more than shorter pulses. Although the present data are consistent with the idea that 1000  $\mu\text{s}$  pulse durations augment the afferent volley, when measured at the level of the spinal cord (via H-reflexes), there was no effect of pulse duration on CS excitability. These results suggest that when a goal of a given NMES therapy is to increase CS excitability to strengthen CS pathways to TA, relatively short or long pulse durations are equally effective.

Presently, the H-reflex was used as an indirect measure of the magnitude of the afferent volley. Although  $H_{\text{max}}$  did not depend

on pulse duration, the current required to produce  $H_{\text{max}}$  (i.e.,  $i_{H_{\text{max}}}$ ), relative to the current required to produce  $M_{\text{max}}$ , was less for the 1000  $\mu\text{s}$  pulses than the shorter pulse durations. This decrease in  $i_{H_{\text{max}}}$  at the longest pulse duration represents a leftward shift in the H-reflex recruitment curve relative to the M-wave curve. This leftward shift is similar to what has been observed for

soleus H-reflexes (Panizza et al. 1989; Lagerquist and Collins 2008) and reflects the generation of a larger afferent volley relative to the efferent volley with longer pulse durations. As such, for a given M-wave amplitude in TA, such as the 10%–15% M-wave used for the NMES sessions in the present study, a larger afferent volley will be sent to the central nervous system when using 1000  $\mu$ s pulse durations than 50 or 200  $\mu$ s pulses.

The effect of pulse duration on the afferent volley has been attributed to the lower rheobase and longer  $\tau_{SD}$  of afferent compared with efferent axons (Veale et al. 1973). These differences in membrane properties may be due to a greater number of persistent sodium channels on afferent axons compared with efferent axons (Bostock and Rothwell 1997) or a relatively more depolarized resting membrane potential for afferents versus efferents (Bostock and Rothwell 1997; Howells et al. 2012). Regardless of the exact mechanism behind the afferent axon's lower rheobase and longer  $\tau_{SD}$ , these membrane properties result in the preferential recruitment of afferents at longer pulse durations (Howells et al. 2012).

Despite the evidence that compared with the shorter pulse durations, a larger afferent volley was generated under the stimulating electrodes by the 1000  $\mu$ s pulses, there was no effect of this enhanced afferent volley on CS excitability. Thirty minutes of NMES increased CS excitability significantly, by ~50%, but this increase was not influenced by pulse duration. We propose that either the differences in the afferent volley between pulse durations were not large enough to influence CS excitability, or there was a small effect of pulse duration but the outcome measure herein (MEPs generated at 1.2 $\times$  RMT) was not sensitive enough to measure it. The rationale for both of these ideas is based on the relatively simple circuitry of the H-reflex, compared with the more complex circuitry that mediates the effect of the afferent volley on CS pathways. It may be that the differential influence of pulse duration on the afferent volley is reflected well in the number of motor units recruited as H-reflexes, but is obscured by integration in ascending pathways and cortical circuits that regulate the strength of the afferent volley that reaches the motor cortex, or by the inherent variability of the excitability cells in the CS pathway. Alternatively, a comparison of MEP recruitment curves collected before and after NMES at the different pulse durations may have provided a more sensitive measure of the influence of pulse duration on CS excitability by testing motor units that represent a larger portion of the motor pool.

In conclusion, the present data are consistent with the idea that compared with shorter pulse durations, 1000  $\mu$ s pulse durations delivered over the CP nerve generate a larger afferent volley relative to the efferent volley. Although this effect was apparent when assessed at the level of the spinal cord, via H-reflexes, the larger afferent volley was not sufficient to significantly increase the excitability of cells in the CS pathway to TA. Because functional improvements associated with NMES have been attributed to increases in CS excitability induced by the electrically evoked afferent volley (Fraser et al. 2002; Everaert et al. 2010), it is important to identify the parameters of NMES that will generate the largest afferent volley and hence the greatest increase in CS excitability. The present results indicate that under the experimental conditions tested herein, although manipulating pulse duration can alter the relative recruitment of afferents and efferents under the stimulating electrodes, longer pulse durations are not different from shorter pulse durations for increasing CS excitability, and thus increasing pulse duration may not be an effective strategy for increasing CS excitability for rehabilitation.

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