Duration of Electrically Induced Muscle Cramp Increased by Increasing Stimulation Frequency

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Context: Electrically induced muscle cramps (EIMC) do not last long enough to study many cramp treatments. Increasing stimulation frequency lengthens cramp duration; it is unknown which frequency elicits the longest EIMC. Objective: To determine which stimulation frequency elicits the longest EIMC and whether cramp duration and stimulation frequency are correlated. Design: Randomized, crossover. Setting: Laboratory. Participants: 20 participants (12 male, 8 female; age 20.7 ± 0.6 y; height 174.9 ± 1.9 cm; mass 76.6 ± 2.2 kg) with a self-reported history of muscle cramps in their lower extremities within the 6 mo before the study. Interventions: The dominant leg’s tibial nerve was percutaneously stimulated with 2-s-duration electrical stimuli trains starting at a frequency of 4 Hz. After 1 min of rest, stimulation frequency increased in 2-Hz increments until a cramp occurred in the flexor hallucis brevis. The stimulation frequency at which a cramp occurred was termed cramp threshold frequency (TF). Cramp duration was determined using strict clinical criteria (loss of hallux rigidity and return of hallux neutral). On the next 4 consecutive days, participants were stimulated at 5, 10, 15, or 20 Hz above TF, and cramp duration was reassessed. Main Outcome Measures: Cramp TF and duration. Results: Cramp TF was 16.9 ± 5.1 Hz. Cramp duration was longer at 15 and 20 Hz above TF (77.9 ± 37.6 s and 69.5 ± 36.9 s, respectively) than at TF (40.8 ± 34.0 s; P < .05). Cramp duration and TF were highly correlated (r = .90). Conclusions: Stimulating at 15 and 20 Hz above cramp TF produces the longest-lasting EIMC.

Keywords: electromyography, neuromuscular system, flexor hallucis brevis, tetany

Skeletal-muscle cramps are a difficult phenomenon to study scientifically because of their spontaneity, unpredictability, and unclear etiology. Scientists have addressed this problem by inducing muscle cramps in laboratory settings with low-frequency electrical stimulation of peripheral nerves.1–4 The minimum stimulation frequency required to elicit cramping under resting conditions has been termed threshold frequency (TF) and appears to be a quantitative method of verifying cramp susceptibility (ie, lower TFs indicate increased susceptibility to cramping and vice versa).2,5

The clinical applicability of cramp-TF measurements is limited. However, we2 previously reported that individuals with a history of exercise-associated muscle cramps have a significantly lower cramp TF than those who self-report never cramping during or shortly after exercise. Moreover, others have observed that cramp TF is lower after an exercise-associated muscle cramp.6 This suggests that those who experience an exercise-associated muscle cramp may be at increased risk of subsequent cramping episodes if they continue exercising. Therefore, TF may be used by clinicians to identify those at higher risk of developing muscle cramps during exercise. After identification of these individuals, clinicians could tailor strategies to help them prevent cramping in the future (eg, training changes or fluid-replacement strategies).

To date, very little experimentally controlled research has been done examining the effectiveness of various interventions on electrically induced muscle cramps. The few studies that have have traditionally used a pre–post experimental design with cramp TF as the dependent variable.3 Such designs are useful for determining prophylactic cramp interventions but may not be as useful for examining direct treatments for active muscle cramps. Using cramp duration as the primary dependent variable in research experiments testing the efficacy of cramp treatments may be a better way to measure treatment effectiveness if cramps can be induced that last long enough to test the intervention.

We believe that the lack of experimentally controlled research on cramp interventions is partially due to the short duration of electrically induced muscle cramps. Previous work has shown that cramps induced at TF range from 4 to 12 seconds.1,4,7 This is a significant limitation for studying cramp interventions because it would be unclear if cramp cessation occurred spontaneously or as a result of the intervention. There is some scientific support that increasing electrical stimulation frequency above cramp TF may solve this problem.1,5,7
Some authors have noted an inverse relationship between the number of stimuli in a stimulus train and cramp TF in the flexor hallucis brevis (FHB). However, it is unclear which frequencies above TF were used to elicit this response, and those authors did not examine the effect of varying stimulation frequencies on cramp duration. Other authors have observed that cramp duration could be significantly increased (from 4 to 20 s) by electrically stimulating the motor point of the abductor hallucis at a frequency 50% higher than TF. However, those authors only stimulated at a single frequency above TF, and 20 seconds is still too short to study many cramp interventions. Moreover, it is unknown if stimulating the peripheral nerve, rather than the muscle’s motor point, would cause a similar effect on cramp duration in the FHB.

Therefore, we asked which stimulation frequency above TF causes the longest cramps and whether cramp duration and stimulation frequency are correlated. We hypothesized that muscle-cramp duration would increase as stimulation frequency above TF increased and that there would be a significant correlation between cramp duration and stimulation frequency.

Methods

Experimental Design

A balanced, randomized, crossover design guided data collection. Our study had 1 independent variable (stimulation frequency) with 5 levels (TF and 5, 10, 15, and 20 Hz above TF). The FHB’s cramp duration (s) and cramp TF (Hz) were the dependent variables.

Participants

A convenience sample of potential participants with a self-reported history of muscle cramping in the lower extremities within the 6 months before the study was recruited from various exercise science classes and word of mouth. Twenty-one individuals volunteered to participate in the research study; 1 individual discontinued participation due to the discomfort of the electrical stimuli. Thus, 20 participants (12 male, 8 female; age 20.7 ± 0.6 y; height 174.9 ± 1.9 cm; mass 76.6 ± 2.2 kg) completed the study. Exclusion criteria included pregnancy, injury to the dominant lower limb within the 12 months preceding the study, or any self-reported neurological, cardiovascular, or neuromuscular disease. Before experimentation, participants were instructed to abstain from exercise or strenuous activity for the duration of the study. The procedures were approved by our university’s institutional review board, and participants provided written informed consent before experimentation.

Instruments

The muscle action potentials of the FHB were collected using the MP150 analog-to-digital system and AcqKnowledge software (v 3.7.3, Biopac Systems, Santa Barbara, CA). Signals were amplified using the TEL 100C (gain set to 5000, Biopac Systems) from disposable, long-term recording electrodes (Biopac, EL502-10) with a center-to-center interelectrode distance of 2 cm. Amplifier impedance was 2 MΩ with a common-mode rejection ratio of 11 dB and a signal-to-noise ratio of 0.75 dB. The EMG signals were sampled at 2000 Hz and band-pass filtered with the low- and high-frequency filters set at 10 and 500 Hz, respectively. The total cramp EMG recording consisted of baseline (1 s), stimulation (2 s), and poststimulus activity (120 s).

A Grass S88 stimulator with an SIU5 stimulus-isolation unit (Astro-Med, Inc, West Warwick, RI) with an 8-mm Ag-AgCl shielded active electrode (Biopac, EL258S) and an 8-cm, square dispersive electrode was used to deliver the train of electrical stimuli to the tibial nerve. Stimulus intensity and duration were set at 80 V and 2 seconds, respectively, as this intensity and duration have been shown to induce muscle cramps in healthy subjects.

Procedures

Participants reported to a laboratory on 5 consecutive days. On the first day of testing, cramp TF was determined. Participants’ leg dominance was determined by having them kick an imaginary ball. The leg used to kick the ball was considered their dominant limb. They then lay supine with their dominant ankle hanging off a table. Standard EMG preparatory procedures were performed at the medial plantar aspect of the foot, area around the medial malleolus, and ipsilateral tibial tuberosity. Two EMG measurement electrodes were placed 2 cm apart over the midbelly of the FHB with a single reference electrode over the ipsilateral tibial tuberosity. After placement, the electrodes were traced with a permanent marker for replication purposes. Subjects were instructed to re-mark these sites between testing sessions if they noticed they were fading.

Participants then had their dominant leg prepared for cramp induction. An 8-mm Ag-AgCl stimulating electrode was placed slightly inferior to the medial malleolus. The tibial nerve was submaximally stimulated 2 to 4 times with 1-millisecond electrical stimuli at 80 V to determine the site around the medial malleolus that caused the greatest hallux flexion. An 8-cm-square dispersive electrode was placed over the lateral malleolus. Electrodes were secured with medical tape and an elastic wrap at these locations.

To induce a cramp and determine cramp TF, participants received 2 consecutive trains of electrical stimuli (1 train/s, no rest intervals between trains) beginning at a frequency of 4 Hz (8 total stimuli on the first trial). If a cramp did not occur at 4 Hz, participants rested for 1 minute and train frequency was increased by 2 Hz. This process continued until the FHB cramped. The minimum electrical stimulation frequency at which a cramp occurred was considered the cramp TF.

A muscle cramp was defined as an involuntary contraction of the FHB immediately after stimulation and was verified by involuntary, sustained great-toe flexion, subject
verifying that a cramp had occurred, and an average EMG
root-mean-square amplitude >2 SDs above the 1-second
baseline EMG average root-mean-square amplitude.4

We chose to study cramping of the FHB for several
reasons. First, the procedures used to cramp the FHB
have been established1–4 and have both high intrasession
(ICC 3,1 > .84)4 and high intersession reliability (ICC 3,1
>.86).1,4 Second, most research on electrically induced
muscle cramps has been done on the FHB. Thus, it
is possible to compare results across studies. Finally,
muscles like the FHB are easier to cramp because of
their small size.

Cramp duration (s) was determined by strict clinical
criteria (ie, loss of FHB rigidity and pain and restoration
of hallux neutrality) and EMG analysis. We confirmed
the time of cramp cessation from our clinical criteria
with the EMG data. The EMG root-mean-square amplitude
at the time point of cramp cessation (from the clinical
criteria) was compared with resting EMG root-mean-square
amplitude to ensure that it was <2 SDs from resting EMG
activity. Cramp duration was the difference between the
beginning of the cramp (ie, end of the electrical stimu-
il and cramp cessation. Participants were instructed to
relax for the duration of the cramp and to let the cramp
proceed for as long as possible. If the FHB cramped for
≥120 seconds, a moderate static stretch was applied to
the big toe to alleviate it.

On subsequent days, participants received electrical
stimulation at 5, 10, 15, or 20 Hz above their cramp TF,
and cramp duration was reassessed.

Statistical Analyses

Mean FHB cramp duration was used for statistical anal-
ysis (NCSS 2001, Kaysville, UT). A repeated-measures
ANOVA was used to assess differences in cramp dura-
tion due to varying electrical stimulation frequencies.
Tukey–Kramer multiple-comparison tests were used
when F values were significant. A Pearson correlation
coefficient was used to describe the relationship between
cramp duration and stimulation frequency. Significance
was accepted when P < .05.

Results

Data are reported as mean ± SD. Cramp TF on day 1 was
16.9 ± 5.1 Hz. Cramps induced at TF lasted 40.8 ± 34.0
seconds. Cramp duration increased as the stimulation
frequency increased above TF (F4,76 = 8.3, P < .001). It
was 91% longer when stimulated at 15 Hz above TF and
70% longer at 20 Hz above TF than at cramp TF (Figure
1; P < .05). Six participants (30%) developed cramps that
lasted >120 seconds after stimulation at 15 Hz above TF,
but only 4 participants (20%) developed these cramps at
20 Hz above TF. In contrast to these higher stimulation
frequencies, only 1 subject (5%) developed cramps of
this duration at TF and 5 Hz above TF, and 2 (10%) at 10
Hz above TF. Cramp duration and stimulation frequency
were strongly correlated (r = .90, P = .03).

Discussion

Increasing stimulation frequency above cramp TF
produced longer-lasting electrically induced muscle
cramps. The greatest increases in cramp duration came
after stimulation at the highest frequencies. Moreover,
it appeared that cramp duration increased incrementally
as stimulation frequency increased until subjects were
stimulated at 20 Hz above TF. For example, stimulat-
ing at frequencies 10 and 15 Hz above TF resulted in a
42% and 91% increase in cramp duration, respectively.
The mild, but insignificant, decrease in cramp duration
observed between 15 Hz and 20 Hz above TF may be
due to antidromic collision between ectopic firing of the
peripheral nerve due to cramp fasciculations and the elec-
tronic stimulation, or it may be due to simple variation
in the measurement of cramp duration (as noted by the
overlapping SDs). Regardless, we observed that cramp
durations can be lengthened to be long enough to test the
effectiveness of many purported cramp treatments (eg,
stretching) by increasing stimulation frequency.

Few studies have quantified electrically induced
muscle-cramp duration after electrical stimulation at
TF or higher stimulation frequencies. Bertolasi et al3
stimulated the tibial nerve with stimuli trains above TF
to study the effects of stretching on cramp alleviation but
did not quantify what frequencies were used to obtain
the reported results or what the effect of increasing the
stimulation frequency was on cramp duration. Serrao et
al3 examined the effect of pain induced by hypertonic
saline injection on cramp TF and used strict clinical
criteria to determine if a cramp had occurred. As a result
of these strict clinical criteria, their TFs were higher
than others who have examined TF.4 It may be inferred
from these observations that Serrao et al3 elicited stronger
cramps by using a higher stimulation frequency, but,
again, those authors did not examine cramp duration.
The only other authors who have attempted to quantify
electrically induced muscle-cramp duration after electro-

cramp stimulation were Minetto et al, who observed that
stimulating the abductor hallucis’ motor point at TF.
resulted in cramps that lasted approximately 4 seconds. Cramp duration could be increased to 20 seconds by increasing stimulation frequency by 50%. However, these relatively short cramp durations would make it difficult to differentiate the effectiveness of an intervention from spontaneous cessation of the cramp.

We observed significantly longer cramp durations at TF (~40 s) despite having cramp TF similar to that of other studies. Discrepancies between our results and others’ may be due to differences in muscle and nerve architecture, point of stimulation (motor point vs peripheral nerve trunk), fatigability of the muscles and nerves/nerve terminals, and methodology for determining cramp duration. Regardless, our data confirm the observation that increasing electrical stimulation frequency significantly increases electrically induced muscle-cramp duration. In fact, many of our participants had to have their cramps alleviated because they persisted for >120 seconds when stimulated at 15 and 20 Hz above TF. Moreover, we have extended the results of Minetto et al by inducing cramps via peripheral nerve stimulation rather than the muscle’s motor point and at a variety of stimulation frequencies in a different muscle. For example, stimulating in 5-Hz increments above TF resulted in stimulating the nerve at frequencies 30% (5 Hz above TF), 59% (10 Hz above TF), 89% (15 Hz above TF) and 118% (20 Hz above TF) higher than TF. Overall, these data and our strong positive correlation between cramp duration and stimulation frequency are consistent with the force–frequency relationship, which states that increased summation (and therefore fused tetanus) occurs as stimulation frequency increases.

Small-diameter-afferent activation may explain why our cramp durations were much longer than previous reports of cramp duration after various frequencies above cramp TF. While our protocol was generally well tolerated, some activation of small-diameter afferents (nociceptors, mechanoreceptors, etc) undoubtedly occurred from the electrical stimulation, muscle contraction/cramp, or both. Serrao et al observed that pain induced by hypertonic saline injection successfully reduced cramp TF and hypothesized that this was due to chemical activation of small-diameter afferents. They also claimed that nociceptive stimulation of latent myofascial trigger points successfully elicits cramping in the gastrocnemius. Stomach a muscle’s motor point, instead of the peripheral nerve innervating the muscle, was anecdotally claimed by Minetto et al to be more tolerable than peripheral nerve stimulation. If small-diameter-afferent activation facilitates alpha-motoneuron excitability through a positive feedback loop as theorized, our model of inducing cramps may have activated more of these afferents and thus maintained alpha-motoneuron output, leading to longer, more intense cramps. Since we did not apply a peripheral nerve block proximal to the point of stimulation, we cannot rule out the possibility that small-diameter-afferent activation contributed to cramp duration. If small-diameter-afferent activation plays a substantial role in determining the duration of electrically induced or other types of cramps, inducing cramps via peripheral-nerve stimulation may be the preferred model for studying cramp interventions since it produces the longest-lasting muscle cramps and may cause greater small-diameter-afferent nerve activation.

Conclusions

Increasing electrical stimulation frequency above TF increases the duration of electrically induced cramps in rested humans. Increases in cramp duration may be due to increased small-diameter-afferent activation. By increasing the electrical stimulation frequency, scientists can induce cramps that last long enough to examine cramp interventions that are claimed to relieve cramps quickly. More research is needed on methods to prolong cramp duration even further to assess the effect of treatments that require longer durations to be effective (eg, IV infusion).

References