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Prior Heat Stress Effects Fatigue Recovery of the Elbow Flexor Muscles

Masaki Iguchi, PhD, PT and **Richard K. Shields, PhD, PT**
Physical Therapy and Rehabilitation Science, Carver College of Medicine, The University of Iowa, Iowa City, IA

Abstract

Introduction—Long-lasting alterations in hormones, neurotransmitters and stress proteins after hyperthermia may be responsible for the impairment in motor performance during muscle fatigue.

Methods—Subjects (n = 25) performed a maximal intermittent fatigue task of elbow flexion after sitting in either 73 or 26 deg C to examine the effects of prior heat stress on fatigue mechanisms.

Results—The heat stress increased the tympanic and rectal temperatures by 2.3 and 0.82 deg C, respectively, but there was full recovery prior to the fatigue task. While prior heat stress had no effects on fatigue-related changes in volitional torque, EMG activity, torque relaxation rate, MEP size and SP duration, prior heat stress acutely increased the pre-fatigue relaxation rate and chronically prevented long-duration fatigue ($p < 0.05$).

Discussion—These findings indicate that prior passive heat stress alone does not alter voluntary activation during fatigue, but prior heat stress and exercise produce longer-term protection against long-duration fatigue.

Keywords

cortical inhibition; low frequency fatigue; central fatigue; peripheral fatigue; heat shock proteins; sex

INTRODUCTION

Neuromuscular fatigue is a multi-mechanistic phenomenon during repetitive use of skeletal muscle. Heat stress typically accompanies repetitive muscle use and plays a pivotal role in the fatigue process.[1] However, little is known about the influence of prior heat stress on human muscle fatigue. Prior heat stress before physical muscle activity is particularly relevant to individuals with spinal cord injury (SCI), because they have an impaired capacity to sweat. [2] Our goal is to explore if prior passive whole body heat stress affects central and peripheral mechanisms of human skeletal muscle fatigue.

There is now strong evidence which indicates that some of the decline in motor performance during prolonged exercise is attributed to the central nervous system (CNS) not being able to generate or maintain optimal neuronal drive to the exercising muscles (central fatigue).[3] Non-invasive stimulation of the primary motor cortex with transcranial magnetic stimulation

Corresponding Author: Richard K. Shields, Physical Therapy and Rehabilitation Science, Carver College of Medicine, The University of Iowa, 1-252 Medical Education Building, Iowa City, IA 52242-1190; richard-shields@uiowa.edu; 319-335-9791; Fax: 319-335-9707.

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(TMS) considerably enhanced our understanding in human motor control in various areas, including muscle fatigue. When TMS is applied while muscle is being fatigued, motor evoked potentials (MEPs) increased, [4–7] and the silent period (SP) duration increased.[4,6,7] These results were interpreted to mean that muscle fatigue increases both excitatory and inhibitory circuits in the motor cortex, [7] although the relationship between these fatigue-related changes in CNS excitability and central fatigue is not fully understood.[8]

When there is an increase in core body temperature with exercise, the capacity to perform exercise is decreased even in young healthy adults.[9–11] A recent study using TMS indicated that the primary motor cortex output becomes suboptimal with fatigue during heat stress compared to when the body temperature is not elevated.[12]

Electroencephalography recordings from the prefrontal cortex of exercising subjects also indicates that hyperthermia decreases subjects' alertness or motivation.[13] From these reports, some suggest that the brain is a primary site responsible for hyperthermia-induced central fatigue. [12–15] However, no previous study, to our knowledge, examined the influence of prior heat stress and recovery on the mechanisms of muscle fatigue.

The precise physiological mechanisms responsible for hyperthermia-induced central fatigue during exercise remain elusive. An increased ratio of central serotonin to dopamine levels is one of the proposed mechanisms.[16] The concentration of prolactin (PRL) in circulating blood has often been used as an indirect marker of central serotonin and dopamine activity, since its release is stimulated by serotonergic activity and inhibited by dopaminergic activity.[17,18] Interestingly, PRL stays elevated for over an hour after prolonged exercise[19] and after passive heat stress,[20] suggesting that central neurotransmitters may be impaired several hours after a prior dose of passive whole body heat stress.

It is reported that young females are more fatigue resistant than young males.[21–24] Although some studies suggest that the majority of the sex difference can be explained by the intrinsic sex-related differences within skeletal muscle, [23,24] others suggest that impairment of voluntary activation (central fatigue) explains, at least in part, the sex differences during fatigue.[21,22] Accordingly, if prior whole body heat stress triggers differential long-lasting central effects based on sex, then fatigue should be accentuated in males exposed to prior heat stress. In addition, the long term effects from two forms of stress (prior heat followed by fatigue task) may induce specific adaptations that are different from a fatigue task that is not preceded by heat stress.

Therefore, the primary purpose of this study was to determine whether prior whole body heat stress has long-lasting (~ 1 hour) effects on subsequent muscle fatigue, and secondarily, whether the effects vary in males and females. We hypothesized that prior whole body heat stress would have lasting adaptive effects on central fatigue, and males would be more susceptible to the central activation impairment after a bout of heat stress.

MATERIALS AND METHODS

Subjects

A total of 25 subjects (12 females) were recruited. Their age, height, and weight were 21.2 ± 2.1 (mean ± standard deviation, SD) and 23.2 ± 2.2 years old, 182.0 ± 11.2 and 167.8 ± 6.2 cm, and 77.2 ± 15.8 and 60.9 ± 6.7 kg for males and females, respectively. Both groups consisted of physically active college students with a similar perception and report of their physical activity level (for SF36 [25] and Baecke Physical Activity [26]). They had no known neurological or musculoskeletal diseases/disorders, and subjects who were actively involved in any passive heat stress method (hot tub, sauna) were excluded. Subjects were asked to

refrain from exhaustive exercise and intake of caffeine 24 hours prior to participation in the study. Each subject participated in two sessions (heat and no heat session) separated by 7 to 10 days. Subjects were asked to log their dietary intake and were encouraged to maintain the same intake for the days of experiments. No differences were detected between days for dietary intake or studies performed on 7 or 10 days. These two sessions were carried out at a similar time of the day for each subject, and the order of participation in the sessions was counter balanced within sexes. The study was approved by the internal review board at the University of Iowa, and all subjects gave written informed consent prior to participation.

Instrumentation and Experimental Set-up

Whole Body Heat Stress Intervention—In order to induce whole body passive heat stress, we developed a custom designed heat stress chamber. Subjects sat in the heat chamber for 30 min. The temperature inside the chamber was set at 73 °C (relative humidity of 10%) at the face level. When subjects participated in the control session, no heat was turned on while they sat in the same heat chamber for 30 min. The temperature for the no heat session was about 26 °C. The heat intervention significantly increased the subjects' core body temperature (infra-red tympanic sensor, ThermoScan IRT 4520 Braun, Germany) and heart rate (HR) (online Polar logging sensor) from 36.6 ± 0.35 to 38.9 ± 0.44 °C and from 83.9 ± 18.6 to 131.4 ± 22.4 beats per minute by the end of the heat session, respectively. The core body temperature was increased 0.82 °C from the baseline temperature of 37.7 °C as measured via a rectal thermister probe (B10014, MSR Electronics GmbH, Switzerland) inserted 10 cm beyond the anal sphincter. The temperature after leaving the heat stress chamber returned to baseline within 30 minutes, at which time we performed the fatigue testing. There were no differences in the temperature between pre-heat and 30 min post-heat in the heat stress group and between 30 min post-heat in the heat stress group and 30 min post-sitting in room temperature in the control group ($p > 0.10$ for both).

The hormonal and protein changes resulting from heat stress is the focus of a subsequent paper in preparation. Briefly, in order to confirm that the heat stress subjects actually induced changes in hormones, especially prolactin (an indirect marker of central fatigue [17,18]), blood samples were collected before and after heat stress.

Electromyography (EMG) Recordings—EMG was obtained using active bipolar surface electrodes (silver-silver chloride discs of 8 mm in diameter spaced 20 mm between centers) for short and long heads of biceps brachii (BBS and BBL, respectively), brachioradialis (BR), and triceps brachii (TB) of the left arm. Only 1 out of the 25 subjects was left handed. The locations of these electrodes were as follows: lateral (BBL) and medial (BBS) to the line between the medial acromion and the cubital fossa at 1/3 the distance from the cubital fossa, at about 2 cm distal to the elbow joint for BR, and at about 50% on the line between the acromion and the olecranon for TB. The skin at these locations was cleaned and mildly rubbed with an alcohol swab. A common ground electrode was placed on the dorsum of the tested hand. The signal was amplified (x 2k), band-pass filtered (20–4k Hz), and sampled at 4k Hz for all the muscles.

Torque Recording—Volitional torque around the elbow was measured using a torque transducer (model 45E15A-U760, JR3, Woodland, CA). Subjects sat on a custom designed chair with a padded seat and metal frame. The transducer was mounted on an adjustable metal bar extending from the metal frame. The transducer had an extended metal plate from its axis, and the axis of a subject's elbow (the lateral epicondyle of the humerus) was aligned with the axis of the transducer. A cuff at the distal end of the metal plate held each subject's wrist, keeping the forearm on the metal plate. Subjects were asked to pull their wrist toward them for elbow flexion or push the wrist away from them for extension. The shoulder was

abducted 70° and horizontally flexed 45°; the elbow was flexed 70° (0°being full extension); and the forearm was midway between full supination and full pronation. Two non-elastic straps were used at the level of the chest and waist to minimize trunk movement. The analog signal from the transducer was sampled at 1k Hz.

TMS—Stimulation of the primary motor cortex was accomplished using a Magstim 200[2] (Magstim Company Ltd., Whitland, Dyfed, UK) with a 7 cm diameter figure-of-eight coil. The coil was positioned tangential to the skull with the handle facing backward so that the current induced in the brain under the junction of the double coil was in the posterior-anterior direction during the rising phase of the monophasic pulse. The ideal position, where the largest MEP was observed in BBL, was found by moving the coil over the head. Once it had been found, the position was marked on a swim cap tightly fitted to the subject's head. The coil was held manually to that position, and great care was taken to stimulate the same position of the head throughout the experiment. The active motor threshold (AMT) was determined as the minimum intensity required to elicit at least 4 of 8 MEPs whose amplitude was 100 micro-volts above the background volitional EMG (2% MVC). The stimulus intensity was then set at 1.8 times the AMT, and this intensity was used throughout the experiment. MEP responses were measured during muscle activation to better control for both cortical and motor neuron pool excitability, and therefore the MEP size becomes less variable.[27] In addition, holding low background muscle activity ensures that changes in response to TMS are not simply a result of differences in subthreshold activation of neurons.[28]

Experimental Procedure

After subjects left the heat chamber, they dried thoroughly, and sat on the custom-designed chair. EMG recording and ground electrodes were placed on the tested arm, and the arm and the trunk were stabilized for torque measurements.

MVC Measurements—After some warm-up contractions, 3 MVCs into flexion followed by another 3 into extension were measured. Extension MVCs were performed only to normalize the antagonist EMG activity during the fatigue task. Subjects were given visual feedback of the exerted torque on a computer screen placed in front of them, and were verbally encouraged. Each MVC was ~5 sec, and a rest of about 1 min was given between each contraction. Two percent of the MVC torque in flexion was then displayed on the computer screen as a horizontal line. Pilot data showed that this approach maximized the sensitivity to TMS.

TMS Measurements—After finding the AMT and setting the stimulus intensity as described above, subjects were asked to maintain a static contraction at 2% of their MVC for ~20 s, during which 3 single pulses of TMS were delivered. Then subjects were asked to perform 2 – 3 flexion MVCs with a rest of about 1 min between. While they were exerting the maximal torque, one single pulse TMS was superimposed on each MVC. Subjects were asked to bring their torque back to the maximal level as quickly as possible after the superimposed TMS.

Fatigue Task—After all the pre-fatigue measurements described above had been obtained, subjects performed a 7-min fatigue task (Fig. 1A). The task consisted of thirty-five 7-s MVCs (epoch =5 MVCs in each minute, Fig. 1B). There was a rest of 3 s between contractions within each epoch. After the 5th contraction of each minute, subjects performed a target contraction (7 s) at pre-fatigue 2% MVC, at which time TMS was delivered. While subjects were performing the 3rd MVC of each epoch of 5 contractions, TMS was superimposed at the mid-point of the contraction. Subjects were verbally encouraged

throughout the task. The computer display provided feedback for all force levels. Investigators also provided verbal cues to help subjects perform the task.

Post-fatigue Task—In order to examine recovery from the fatigue task, at 1 and 10 min post fatigue one 7-s MVC followed by a 7-s target contraction at 2% (3-s rest between) was performed with TMS superimposed on each contraction.

Data Analyses

All the analog signals were digitized and analyzed using Datapac 2K2 ver. 3.18 (Run Technologies Co., CA). Pre-fatigue and post-1 and 10 min MVC torque and EMG activity were determined by taking the mean and root mean square (RMS) amplitude of the torque and EMG signals, respectively, of a 2-s window where the torque was stable. For trials on which TMS was superimposed (post 1- and 10-min MVCs), 2 separate time windows were used before and after TMS, so TMS-induced extra torque (if any) and stimulus artifacts were not included. The higher value from the two windows was chosen to represent the maximal torque and EMG for that trial. During the fatigue task, volitional torque and EMG were calculated as mean and RMS amplitude of the middle 4 s for each 7-s MVC, and 5 values from each minute were averaged. Both peak-to-peak and integrated amplitude (between 10 ms and 40 ms after TMS, Fig. 1D) were used to quantify the MEP size, but only the peak-to-peak amplitude is reported in the results because these two measurements were highly correlated (R value = 0.93). The pre-stimulus EMG activity was determined by calculating the RMS amplitude of the 100-ms EMG signal immediately before TMS delivery, and this was used to normalize the MEP size. Although TMS was delivered both on MVCs and on the 2% MVC target contractions (Fig. 1B), SP duration and peak torque relaxation rate were quantified during the MVCs only. SP duration was determined as the time between the TMS delivery and the recurrence of continuous voluntary EMG activity after TMS using visual inspection. It has been recently reported [29] that the visual inspection approach to quantify the SP duration results in slightly lower between-visit variability than the mathematical approach described elsewhere.[30] The peak relaxation rate was calculated as the maximal rate of decline in torque during SP.[31] This was done by first calculating the slope of a regression line (25 ms) computed for successive moving intervals over the duration during which the voluntary torque was declining after TMS, and then the minimal slope (due to the torque decline) was chosen as the peak relaxation rate. Negative values of the rate were expressed as positive, so a decrease in the value indicates slowing of the rate of muscle relaxation. In order to account for the difference in rate with different torque levels, the peak relaxation rate was divided by the peak torque from which the torque started to decline. Whenever possible, values obtained during and after the fatigue task were expressed as a percentage of the corresponding value from the pre-fatigue measurements.

Statistical Analyses—In order to determine whether heat stress alone had any effects on the dependent variables, pre-fatigue measurements were compared using repeated measures 2 × 2 (sex as the between-subjects independent variable and heat/no heat as the within-subjects independent variable) analysis of variance (ANOVA). Although the heat intervention preceded the fatigue task only in the heat session, the level of agreement for each of the pre-fatigue variables was assessed across sessions using intraclass correlation (ICC) analyses. Dependent variables obtained during and after the fatigue task were analyzed using three-way ANOVA to determine whether time, sex and intervention had significant effects. A significance level of 0.05 was used for all statistical analyses. Results are reported as mean ± SD in the text and table, whereas figures show the means with standard error.

RESULTS

Prior whole body heat stress induced significant changes in blood plasma markers for heat stress proteins (HSP72), prolactin (PRL), and norepinephrine (NE) (Table 1). These findings confirm that our dose of passive heat stress produced changes similar to other reports.[20] Importantly, the heat-induced increase in body temperature had returned to baseline before the fatigue task was performed (see Whole Body Heat Stress Intervention in Materials and Methods).

Pre-fatigue Measurements

Table 2 shows results from the measurements after either the no heat or heat intervention, but before performing any fatiguing muscle contractions. Heat did not affect ($p > 0.05$) the baseline MVC torque, AMT, MEP size on the target contraction or SP duration on the MVC. However, heat increased ($p < 0.05$) the maximal relaxation rate in both sexes. The MVC torque was lower ($p < 0.01$), and the relaxation rate was slower ($p < 0.05$) for females than those of males in both sessions. The ICC analyses performed on each of the pre-fatigue dependent variables across sessions ranged from 0.75 (SP duration of BBL) to 0.97 (MVC torque). These moderately high values indicate that the prior heat condition caused no acute affect on the pre-fatigue measurements.

Voluntary Torque and EMG Activation Levels

Voluntary torque decreased significantly in the first half of the 7-min fatigue task, and then gradually toward the end of the task (Fig. 2). The torque decrease with time was similar across sessions for both males and females. However, there were interactions ($p < 0.01$) of “sex” × “time” in both no heat and heat sessions. The torque of females, when expressed as a percentage of pre-fatigue values, was higher ($p < 0.05$) than that of males in both sessions after about 1/3 of the task. The quick recovery after a rest of 1 min was similar for all conditions.

During the fatigue task, the biceps brachii showed relatively constant EMG activity, whereas the BR showed a gradual decrease with time. The BR activity decreased significantly with time in all conditions during the fatigue task (Fig. 3C), but there was no main effect of “session” in either males or females. The decrease in BR activity was less in females than in males, resulting in significant differences between males and females at the end of the fatigue task in the no heat session. BBS activity of the males did not change significantly during the task with no session effect (Fig. 3A). In females, the BBS activity decreased only in the no heat session (significant main effect of “time” in no heat, but not in heat). The behavior of BBL was similar to that of BBS (Fig. 3B). The BBL activity decreased significantly with time only in males in both no heat and heat sessions (no significant main effect of “time” in females). No heat effect was found in either males or females in BBL, but there was a significant main effect of “sex” during the heat condition, resulting in significant differences between females and males at the 5^{th} and 7^{th} min. Although all EMG activity recovered with time after completion of the fatigue task, no differences were found between males and females or between no heat and heat sessions in any muscles. The antagonist, TB stayed consistent at 10% of its pre-fatigue MVC level throughout the fatigue task, and there were no main effects of “time”, ”sex” or ”session” (data not shown).

Central Cortical Excitability: Motor Evoked Potential (MEP) Size

The RMS amplitude of the EMG signal immediately before TMS on the target contractions stayed at ~ 1 – 2% MVC level throughout the task for all muscles (no main effect of time in any muscles), and there was no difference across groups or across sex. The size of MEPs recorded on the target 2% MVC contractions (Fig. 1C) increased with fatigue in all flexor

muscles in all conditions (Fig. 4). However, the MEP size was not affected by either heat or sex. When the MEP size was normalized to the pre-stimulus EMG activity, the results did not change. The MEP size of flexor muscles during MVCs (Fig. 1D) was also analyzed, but results were similar to those elicited with the 2% target contractions. The MEP of the TB on flexion MVCs remained negligible throughout the fatigue task.

Central Cortical Inhibition: Silent Period (SP) Duration

Fatigue increased the duration of SP in both sessions (Figs. 1D and 5). During and after the fatigue task, SP durations of all the flexor muscles behaved similarly across sessions and across sexes (no "sex" or "session" effect with no interactions, $p > 0.05$). Although SP duration recovered with rest (post-1 and 10 min), there was no "sex" or "session" effect.

Peripheral Muscle Changes: Relaxation Rate

The peak relaxation rate was decreased with fatigue (Figs 1D and 6), but the absolute rate was higher for males than females at the start of the fatigue protocol ($p < 0.01$). At 2nd min, the relaxation rate in all conditions was similar ($p > 0.05$), and this was the case to the end of the task. At the post-10 min time, the rate of muscle relaxation was again higher for males ($p = 0.01$) than for females. The effect of heat was not significant ($p > 0.05$).

Effect of Heat/Fatigue Test Order on Long Duration Muscle Fatigue

Half of the subjects participated in the no heat session prior to the fatigue test as their 1st session, and one week later they experienced the heat session and fatigue test. Conversely, the rest of the subjects participated in these sessions with a reversed order in that at the first session they experienced the heat and fatigue test and one week later they experienced only the fatigue test. Volitional torque recovered faster ($p < 0.05$) at 1- and 10-min in the group that experienced the heat and the fatigue test one week prior (1-min post fatigue (% pre-fatigue) = 75.7 ± 18.6, 64.7 ± 11.2, 62.5 ± 15.4 and 64.1 ± 17.4 and 10-min post-fatigue (% pre-fatigue) = 82.5 ± 19.9, 69.8 ± 16.9, 71.6 ± 16.4, 74.3 ±15.9 for fatigue test 1 week after heat/fatigue test, fatigue test day 1, heat/fatigue test day 1 and heat/fatigue test 1 week after fatigue test, respectively; Fig. 7A, B). This greater recovery from muscle fatigue was consistent in both the male and female cohorts (Fig. 7A, B).

DISCUSSION

The main purpose of this study was to investigate whether the previously reported hyperthermia-induced central fatigue [9–12] is long-lasting and independent of exercise. The second aim was to investigate whether males and females behave differently to fatigue after heat stress, since it has been shown that females are more fatigue resistant compared to males.[21,22,32,33] Lastly, we aspired to probe into long term (1 week) adaptations when subjects were exposed to two versus one form of stress. The main findings of the study were: 1) males fatigued more than females but prior heat had no significant effect on torque decline, 2) the muscle contractile property (the peak relaxation rate) showed a greater fatigue-induced change in males than females, 3) the whole body heating did not influence the MEP size and SP duration before or after fatigue, and 4) a single bout of heat stress and fatiguing exercise delivered a week prior caused greater recovery in torque after muscle fatigue.

TMS Responses with Fatigue and with Heat

Although fatigue causes changes at multiple sites along the motor pathway from the cortex in the brain to the muscle sarcolemma, [3,34–36] there are several studies which indicate that

the changes we observed in MEP size[34,37] and SP duration[7,38] are primarily of cortical origin.

In our study, whole body heating was applied before the fatigue task. Altered temperature with heating can change the properties of muscle fiber action potentials. The effect of temperature seems minimal, since our pilot study has shown that the skin temperature decreases rapidly after leaving the heat chamber, therefore, by the time the data collection started, skin temperature was similar for control and heat sessions. The reproducibility of the pre-fatigue dependent variables between groups in this study further indicates that conditions recovered quickly following heat stress.

Sex Difference in Muscle Fatigue

It has been shown that young females are more fatigue resistant than young males in certain fatigue tasks. Many of the proposed mechanisms for the sex difference in muscle fatigue lie within skeletal muscles.[39–43] In this study, only peak relaxation rate provides information regarding muscle peripheral changes during fatigue. Males had a significantly higher muscle relaxation rate before fatigue, and this was negatively correlated with the extent of fatigue in the no heat session. Our previously reported [24] findings suggest that the contractile speed of a muscle alone can predict to some extent how much fatigue subjects are going to experience.

Previous studies have reported inconsistent results regarding whether there is a difference in the extent of central fatigue between males and females. In the ankle dorsiflexors [22] and knee extensors,[21] males showed greater central fatigue than females, but no sex differences in central fatigue were found in the elbow flexors.[23] In our study, although the relative decrease in torque was greater in males compared to females, neither MEP size nor SP duration showed differences between sexes during the fatigue task, indicating that the extent of fatigue-induced increases in intracortical inhibition and cortical excitability were similar for males and females, consistent with the finding of Hunter and colleagues.[23]

One of the proposed mechanisms for greater muscle fatigue in males compared to females is a sex difference in activity of group III and IV muscle afferents.[22] The absence of differences in MEP size between sexes in our study indicates that the excitability of the motor pathway did not differentially change for males and females. Amann and colleagues have emphasized the critical role of somatosensory feedback from working muscles on centrally mediated determination of central motor drive.[44] However, recently the notion that increased group III and IV muscle afferent activity reduces motoneuron excitability has been questioned in the elbow flexors,[36,45] and therefore, it is not clear what role, if any, the small diameter muscle afferents have during fatigue.

Prior Whole Body Heating and Muscle Fatigue

Whether prior whole body heating has any long-lasting effects on human muscle fatigue was a central thesis of this study. The rationale for this study was grounded in the construct that prolactin, an indirect marker of central fatigue, has been shown to stay elevated (~ 60 min) after stress.[19,20] We confirmed that the current heat stress intervention caused a nearly 4-fold increase in prolactin. Taken together, these previous findings raised the possibility that central fatigue could “carry over” after selective changes in CNS chemistry (prolactin is an indirect indicator of neurotransmitters) in the absence of exercise.

Previous studies have found that whole body heat stress exaggerates the decrease in torque during fatiguing contractions compared to when no heat stress is applied.[11,12,46] However, most of these studies examined fatigue during heat stress and not after a prior bout of heat stress and recovery. One of the studies that investigated fatigue during heat stress [12]

suggests that the heat-induced central fatigue was due to the inability of the central nervous system to maintain the firing frequencies necessary to generate fully fused contractions.

Increased brain temperature during exercise has been reported to be a clear perturbation in performing exercise, [1,11] but an increase in contractile speeds with heat would create an even more challenging situation for the CNS to maintain maximal voluntary contractions. We did not observe significant differences in the relaxation rate between sessions during the fatigue task (Fig. 6), and therefore, prior heat-induced peripheral changes in muscle (contractile speeds) did not contribute to the development of central fatigue in this study. It has been suggested that hyperthermia-induced central fatigue functions to prevent a further increase in body temperature, so that any dangerous conditions such as heat stroke can be avoided.[14,47–49] If this is true, the heat-induced detrimental effect on muscle fatigue should recover quickly as the body temperature returns to a normal, pre-heated level. This suggests that the long-lasting changes in neurotransmitters (serotonergic inhibitors) do not directly cause heat-induced central fatigue, as has often been postulated. It is possible that long-lasting changes in neurotransmitters act in combination with other mechanisms that become saturated during an intense fatigue task as performed in this study. It may be that by allowing the body to cool down, acute primary signaling to the hypothalamus recovers,[50] and the longer term changes in neurotransmitters (i.e. serotonin-dopamine) alone does not preferentially affect central fatigue during an isolated fatigue task.

We did not find any differences in EMG responses to TMS between heat and no heat sessions. This is consistent with the only previous study that used TMS during a fatigue task under hyperthermic conditions.[12] This prompted the authors to conclude that the site responsible for the heat-induced central fatigue is “upstream” of the primary motor cortex. Interestingly, rest after muscle fatigue is associated with recovery from any EMG changes related to repetitive activation of the motor pathway (changes in MEP size and SP duration) even when the fatigued muscle was kept ischemic (and therefore increased activity of group III and IV muscle afferents).[8] Conversely, supraspinal fatigue (increased interpolated twitch) did not improve until blood flow to the muscle was restored.[8] These findings suggest that small diameter muscle afferents can reduce voluntary activation without impairing the excitability of the motor pathway from the primary motor cortex to the muscle fibers. Accordingly, the mechanisms responsible for central fatigue are likely multi-mechanistic and involve “online” peripheral inputs as well as central components. Hence, in this study, we induced central systemic changes, but once the fatigue protocol ensued, peripheral signaling may have become more prominent. It may be that systemic changes as a result of passive heat stress will have a greater impact on “central fatigue” during aerobic whole body exercise rather than on anaerobic isolated muscle fatigue as performed in this study.

Long-lasting Effect of Heat Stress and Exercise on Recovery from Muscle Fatigue

The extent of the torque recovery after fatigue was greater in the 2nd no heat session compared to that seen in any other conditions. It does not seem that heat stress had any acute (~ 1 h) effect on muscle fatigue since the torque decline and recovery was similar in the heat and no heat sessions. Similarly, fatiguing exercise performed a week in advance without prior heat stress had no significant effect on the torque recovery. Therefore, our data indicates that two stressful events (heat stress and fatiguing exercise) combined caused a “protection” that enabled the torque to recover in both males and females.

This significant recovery was unexpected and raised several possibilities to consider. First, no significant differences existed in baseline torque measures between days. Moreover, all dependent variables changed similarly during fatigue. Thus, we suggest this effect was a protective adaptation associated with the dose of stress delivered. One of the protective responses triggered with stress is the induction of stress proteins known as heat shock

proteins (HSPs). When cells are exposed to sub-lethal stress, inducible forms of HSPs are up-regulated, resulting in the acquisition of greater stress resistance.[51] In fact, the HSP level has been reported to be increased markedly 2–7 days after a single bout of non-damaging, aerobic exercise in exercised skeletal muscles.[52,53] Because HSPs are known to be up-regulated by various forms of stress,[51] it is possible that the heat stress applied before the fatiguing exercise in the first heat session may have enhanced the induction of HSPs in the muscle compared to the fatiguing exercise alone. The torque in the 2nd no heat session differed from that of other sessions only in the recovery from muscle fatigue. This may be due to a protective role of HSPs on low-frequency fatigue (a preferential decrease in the force elicited with electrical stimulation at a low frequency, compared to a high frequency).[54,55] After the strenuous repetitive MVCs, it is possible that the elbow flexors experienced low-frequency fatigue to some extent in all conditions. Low frequency fatigue has been attributed to compromise of excitation-contraction coupling,[55] and it has been suggested that HSPs may be involved in modulation of the excitation-contraction coupling process.[56] Further study is underway to determine if a dose of passive heat stress plus exercise translates into a strategy to offset long duration fatigue.

Clinical Implications

Individuals with paralysis have a limited capacity to generate repetitive muscle force after SCI.[57–61] Moreover, individuals with SCI lose the ability to sweat and shiver, which causes rapid shifts in core body temperature based on the environment.[2] Consequently, an elevated body temperature in a warm climate may shift below normal when a cooler environment is entered (e.g. air conditioning). The ability for individuals with SCI to use their intact upper extremities after an acute dose of heat stress is unknown. This study suggests that a dose of heat stress minimally influences central drive and peripheral muscle fatigue in those with intact central nervous systems, however the effect on those with impaired nervous systems remains unknown. Finally, isolated repetitive exercise after an increase in core body temperature may render the upper extremity muscles of those with paraplegia resistant to prolonged fatigue.

Low-frequency fatigue may also contribute to injuries in sporting events,[62,63] and it has been known that heat shock protein induced in skeletal muscle attenuates the extent of low-frequency fatigue.[56] If a combination of passive heat stress and fatiguing contractions is a viable method to induce Hsp greater than fatiguing exercise alone, this could be used as a preventive procedure for human performance-related injuries. Future studies need to investigate this possibility, and associated physiological mechanisms.

Summary and Conclusions

Whole body heat stress had a minor influence on human muscle fatigue after the increased body temperature had returned to baseline levels. Although females fatigued less compared to males, the decrease in torque was similar before and after heat for either sex. However, torque recovery from muscle fatigue was improved if heat stress and fatiguing exercise were performed a week before, suggesting that these stressful events led to a long-lasting recovery effect on muscle fatigue. The precise mechanisms contributing to this effect require further study.

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Abbreviations

AMT	active motor threshold
ANOVA	analysis of variance
BBL	biceps brachii long head
BBS	biceps brachii short head
BR	brachioradialis
CNS	central nervous system
EMG	electromyography
HR	heart rate
HSP	heat shock protein
ICC	intraclass correlation
MEP	motor evoked potential
MVC	maximal voluntary contraction
PRL	prolactin
RMS	root mean square
SCI	spinal cord injury
SD	standard deviation
SP	silent period
TB	triceps brachii
TMS	transcranial magnetic stimulation

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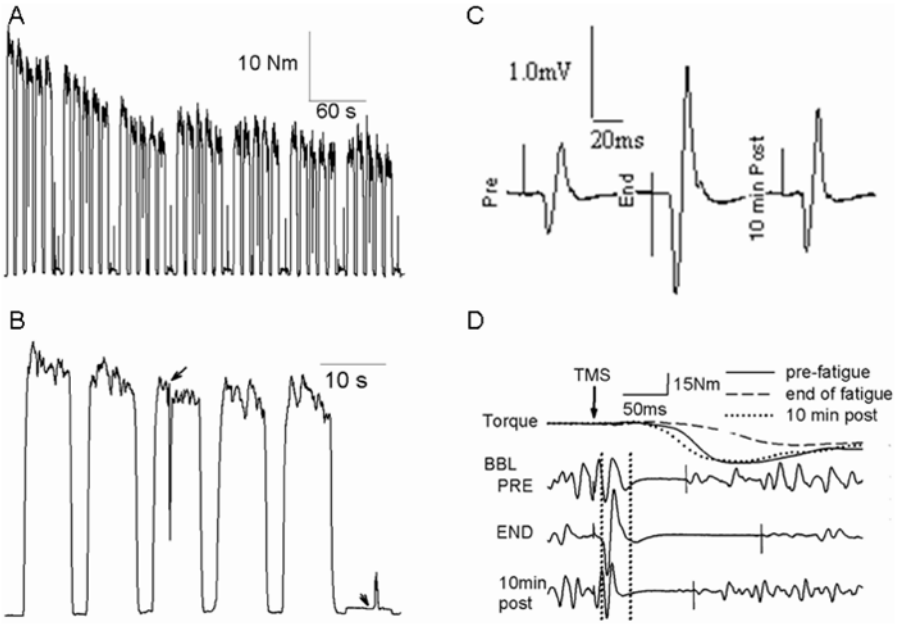

Figure 1.

Representative examples of volitional torque during the 7-min fatigue task (A), an expanded signal of the torque showing only the 1st minute (B), MEPs (in BBL) recorded on the target 2% MVC (C) and torque and BBL EMG responses after TMS superimposed on MVC (D). Subjects performed five 7-s MVCs, followed by a 7-s target contraction at pre-fatigue 2% MVC for each minute. TMS was delivered on the 3rd MVCs and on the target contractions, which are indicated by arrows in B. In D, the torque immediately before TMS has been off-set for clarity purpose. The arrow and the two vertical dotted lines indicate the time of TMS delivery and the time window used to calculate the integrated amplitude for the MEP size, respectively. The short solid vertical lines on the EMG signals indicate the termination of the SP.

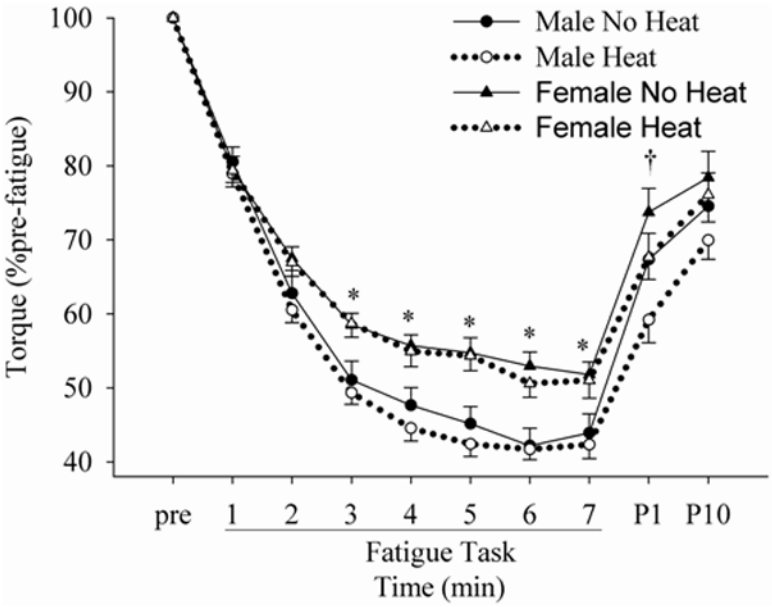

Figure 2.

Changes in the normalized torque during and after the fatigue task in no heat and heat conditions. pre, P1 and P10 indicate pre-fatigue, post 1- and 10-min. * indicates differences ($p < 0.05$) between males and females. † indicates a difference ($p < 0.05$) between no heat and heat sessions when males and females were pooled.

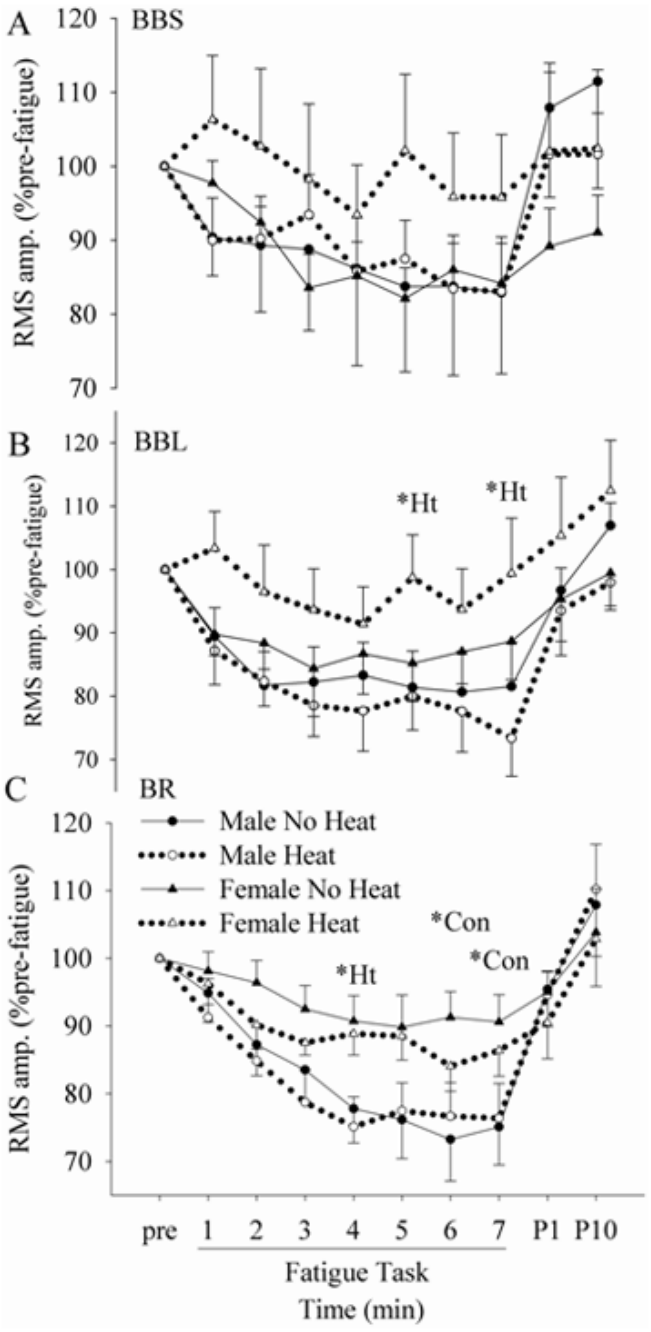

Figure 3.

Changes in the EMG RMS amplitude of BBS (biceps brachii short head, A), BBL (biceps long head, B), and BR (brachioradialis, C) during and after the 7-min fatigue task in no heat and heat sessions. $*^{Ht}$ = differences between females and males in the heat session. $*^{Con}$ = differences between females and males in the no heat session

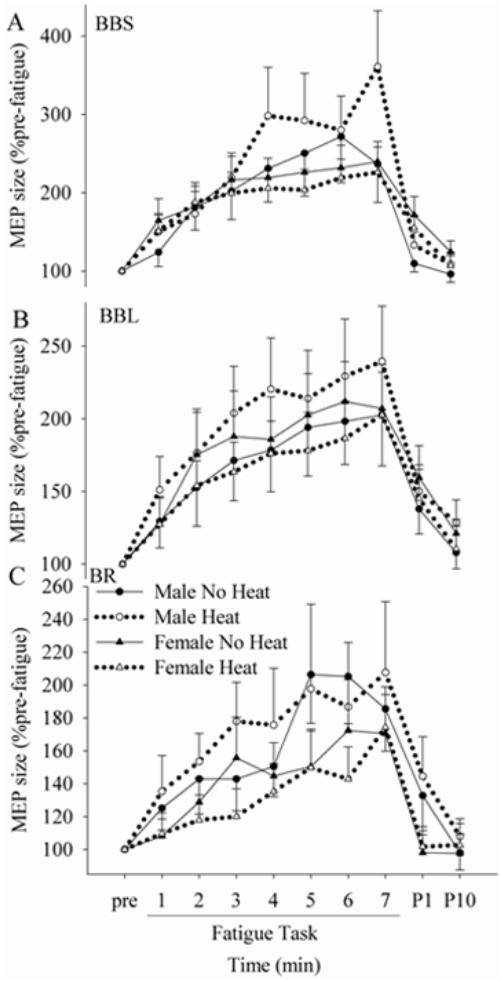

Figure 4.

Changes in the MEP size on the target contraction in BBS (A), BBL (B) and BR (C) during and after the fatigue task in no heat and heat conditions. Although fatigue increased the MEP size, how it increased was similar across sessions and across sexes.

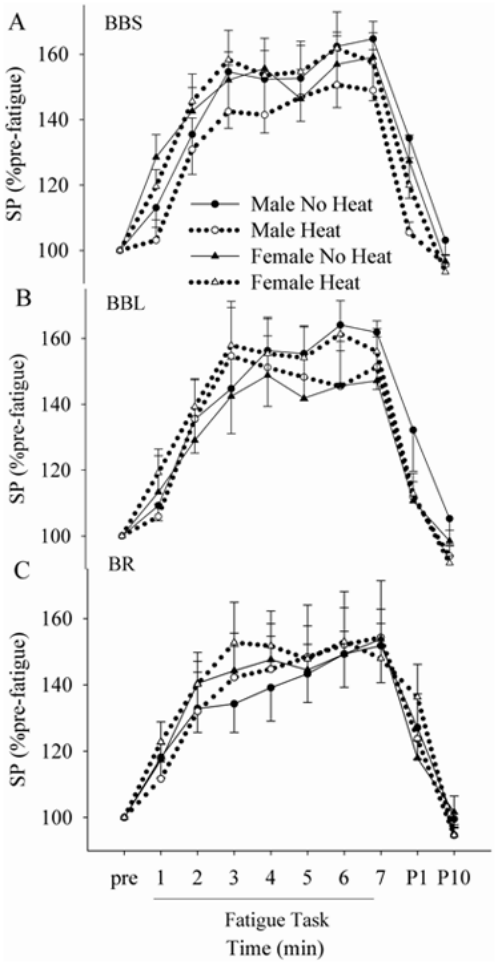

Figure 5.

Changes in the SP duration in BBS (A), BBL (B) and BR (C) during and after the fatigue task in no heat and heat sessions. No ($p > 0.05$) "sex" or "session" effect was found in any of the muscles.

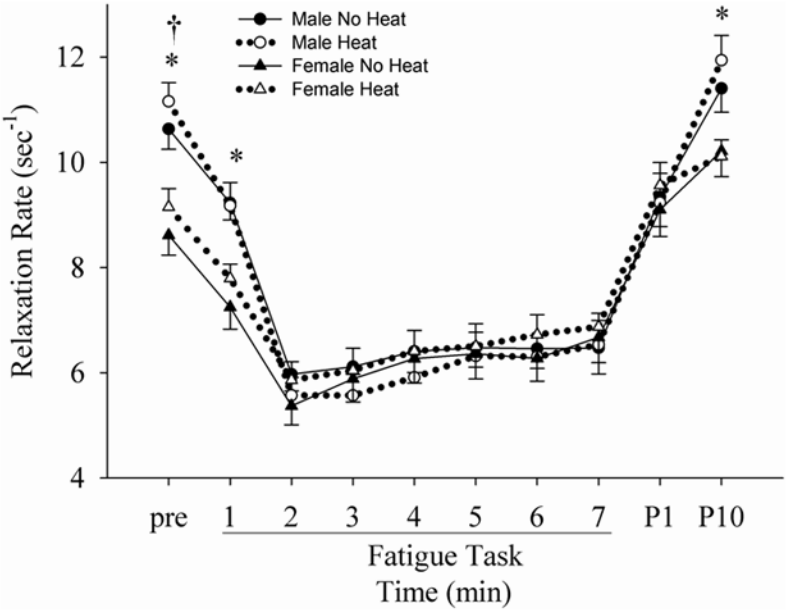

Figure 6.

Changes in the normalized (to the torque before the torque decline) peak relaxation rate of the voluntary torque before, during and after the fatigue task in no heat and heat sessions. *: differences between males and females in both sessions. †: difference between no heat and heat sessions in both males and females.

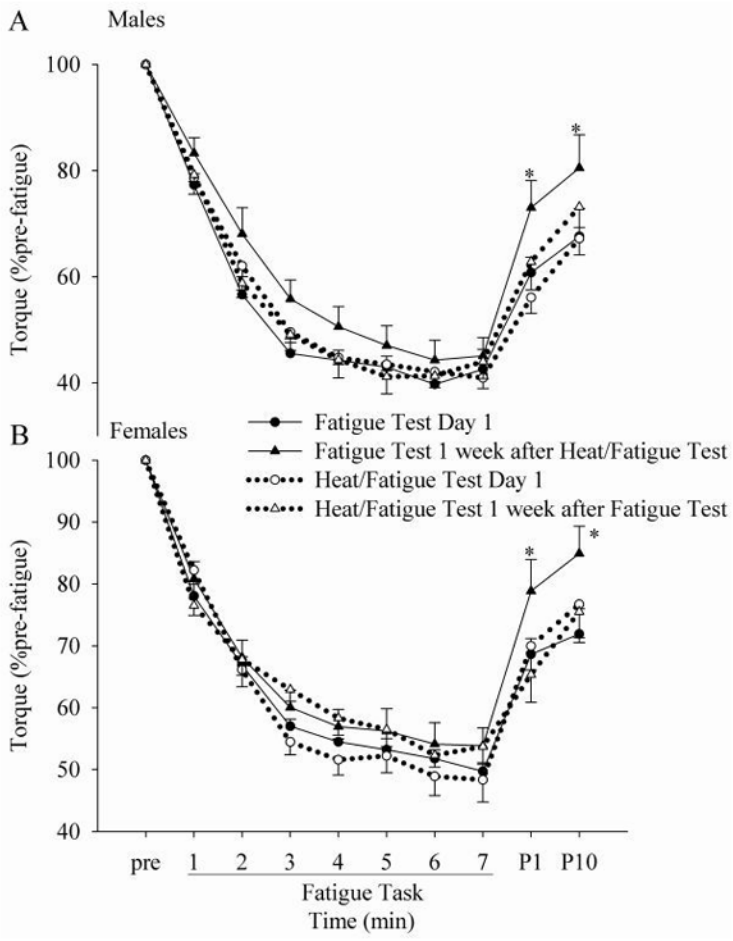

Figure 7.

Changes in the normalized torque for each session (A for males and B for females). Half of the subjects (6 males and 6 females) participated in the no heat session first (Fatigue Test Day 1), followed by the heat session (Heat/Fatigue Test 1 week after Fatigue Test), while the rest of the subjects (7 males and 6 females) participated in these sessions with a reversed order (Heat/Fatigue Test Day 1 followed by Fatigue Test 1 week after Heat/Fatigue Test). * indicates differences in the torque in the Fatigue Test 1 week after Heat/Fatigue Test from that of other conditions.

Table 1

Absolute concentrations of stress protein and hormones before and after the heat stress.

Protein and hormones	Before Heat	After Heat
HSP72 (ng/ml)	2.82 ± 2.07	3.79 ± 2.29 *
PRL (ng/ml)	7.60 ± 4.29	25.7 ± 11.8 *
NE (pg/ml)	523.3 ± 237.2	768.9 ± 333.7 *

HSP72 = heat stress protein 72. PRL = prolactin. NE = norepinephrine.

The asterisks indicate that there were significant ($p < 0.05$) increases after the prior passive heat stress. The whole body heat stress at 73 deg C for 30 min increased the HSP72, PRL and NE levels.

Table 2

Results (means ± SD) of measurements done after either the heat or no heat conditions, but before any fatiguing muscle contractions.

Variables	Sex	No Heat	Heat	ICC
MVC torque (Nm)	Males	63.6 ±13. 5 *	65.9 ± 12.7 *	0.9661
	Females	33.7 ± 4.8	33.9 ± 5.8	
AMT (%MSO)	Males	49.1 ± 5.8 *	48.9 ± 6.4 *	0.7735
	Females	43.9 ± 6.2	43.5 ± 4.9	
MEP amplitude (mV)	Males	BBS 0.94 ± 0.66	BBS 0.79 ± 0.61	0.9474
		BBL 1.06 ± 0.64	BBL 0.97 ± 0.70	0.9516
		BR 0.36 ± 0.23	BR 0.33 ± 0.29	0.7978
	Females	BBS 0.82 ± 0.77	BBS 0.92 ± 0.84	
		BBL 1.02 ± 0.64	BBL 1.09 ± 0.58	
		BR 0.51 ± 0.38	BR 0.61 ± 0.69	
SP duration (ms)	Males	BBS 149.9± 56.7	BBS 146.5 ± 48.4	0.7898
		BBL 147.3 ± 58.9	BBL 142.3 ± 52.1	0.7542
		BR 165.0 ± 50.0	BR 157.7 ± 48.3	0.8624
	Females	BBS 122.1 ± 49.2	BBS 112.6 ± 34.2	
		BBL 133.0 ± 51.5	BBL 112.7 ± 37.0	
		BR 136.8 ± 35.8	BR 130.6 ± 39.4	
Relaxation rate (sec^{-1})	Males	10.6 ± 1.4 *, †	11.2 ± 1.3 *	0.7827
	Females	8.6 ± 1.3 †	9.2 ± 1.2	

No interaction ($p > 0.05$) of "sex" × "session" was found in any comparisons.

* differences ($p \leq 0.05$) between sexes within sessions.

† differences ($p < 0.05$) between sessions within sexes. ICCs were calculated using data from both sexes.

MVC = maximal voluntary contraction. AMT = active motor threshold. MSO = maximal stimulator output. MEP = motor evoked potential (on the target 2% MVC). SP = silent period. ICC = intraclass correlation coefficient