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## Motor performance is preserved in healthy aged adults following severe whole-body hyperthermia

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### ABSTRACT

Healthy aging is associated with a progressive decline in motor performance and thermoregulatory efficiency. Functional consequences of severe whole-body hyperthermia on neurophysiological functions in healthy aged men have not been investigated. To determine whether severe whole-body hyperthermia (increase in rectal temperature of about 2.5 °C) induced by lower-body heating in older men (64–80 years,  $n = 9$ ) would suppress excitability of reflexes, voluntarily and electrically induced ankle plantar flexor contractile properties were compared with those in young men (19–21 years,  $n = 11$ ). Though no aging effect on hyperthermia-induced reflex amplitudes was observed, a decrease in maximal H-reflex and V-wave latencies was found to be greater in older than in young men. In older men, lower-body heating was accompanied by a significant increase in twitch and tetani test torque in parallel with a greater decrease in muscle contraction time. There was no temperature-dependent aging effect on the voluntary activation and maximal voluntary torque production. Despite delayed and weakened thermoregulation and age-related decline in neuromuscular function, motor performance in whole-body severe hyperthermia is apparently preserved in healthy aging.

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Heat stress; reflexes; aging muscle; electromyography (EMG)

## 1. Introduction

As we age, motor performance [1] and thermoregulatory efficiency [2] progressively declines, creating job-related health and safety concerns. Age-related progressive decline in neuromuscular function, characterized by reduced force generating capacity, loss of muscle mass (sarcopenia) [3,4], loss of neuron fiber size and density [5], is highly predictive of frailty, disability, and mortality [6,7]. Moreover, decrements in whole-body heat loss responses, such as decreased sweating and skin blood flow, predisposes older individuals to hyperthermia in a hot environment [8,9] and compromises their ability to thermoregulate during work or exercise in the heat [9]. Most studies have used passive direct (e.g. water bath) or indirect (e.g. water-perfused suit) external heating of older subjects and have focused on the direct effects of mild-to-severe whole-body hyperthermia (WBH) on the kinetics of physiological responses including body temperature [2], sweating efficiency [10], cardiovascular parameters [11,12], metabolic rate [2], heat gain [2,10], subjective sensation [13], and cognition [14]. To our knowledge, the functional consequences of severe WBH (rectal temperature increase from normal  $\geq 1.5$  °C; Bain, Nybo [15]) on neurophysiological functions in healthy aged men have not been fully investigated.

Evidence indicates that severe WBH impairs peripheral motor drive in young adults [16,17] and this impairment in

spinal modulation of neural drive was, in part, attributed to temperature-sensitive groups III and IV afferents [18–20]. As these afferent (sensory) fibers are affected before efferent (motor) fibers by age (21–29 vs. 63–80 years old) [21,22] and considering in aged nerves acquiring Na<sup>+</sup> channelopathy, with ectopic expression of NaV1.8 isoform on motor axons [23], the activity of which is temperature-dependent [24,25] severe WBH might stress neuromuscular physiology, lead to a greater presynaptic inhibition or disturbance, and consequently cause greater impairment of spinal or supraspinal motor drive (i.e. H- and V-wave) in older men than in young men. If so, one would expect that impaired spinal reflex response in older men by severe WBH would contribute to a greater decrease in maximal voluntary contraction (MVC) torque production and central voluntary activation (central activation ratio, CAR) level of exercising muscle.

It has been proposed that attenuated neural excitability associated with a weaker electrically induced torque development potentially contributes to a postural instability with advanced age [22]. Age-related loss of muscle mass and force, and slowing of contractile speed and rate of muscle relaxation, contributes to peripheral muscle effects, including slowing of sarcoplasmic reticulum (SR) ATPase activity and utilization [26], slowed Ca<sup>2+</sup> release and uptake rate from the SR [27], delayed or slower cross-bridge formation, and detachment [28], and decreased actomyosin sensitivity to

Ca<sup>2+</sup> [29]. A molecular basis of contractile apparatus dysfunction occurring with age is increased levels of reactive oxygen species (ROS) in the aged muscle, which are associated with altered cellular Ca<sup>2+</sup> handling. Hyperthermia in ryanodine receptor 1 (RyR1) produces a leak of Ca<sup>2+</sup> from the SR, which promotes mitochondrial dysfunction and oxidative stress-mediated changes of the RyR1 [30], resulting in channels that can leak SR Ca<sup>2+</sup>, leading to reduced SR Ca<sup>2+</sup> release, myofibrillar Ca<sup>2+</sup> sensitivity, and overall loss of muscle function [31]. Leaky RyR1 contributes to age-related loss of muscle function [32]. However, it can be expected that in older individuals, mainly because of attenuated thermoregulation [2] and muscle function [28,29] more heat will be accumulated and stored in the heated locations and the body core, resulting greater metabolically induced mitochondrial ROS production [33], leading to reduced Ca<sup>2+</sup> kinetics and overall loss of muscle function [30].

Therefore, the primary purpose of our study was to determine whether severe WBH (increase in  $T_{re}$  of approximately 2.5 °C from baseline) induced by lower-body heating in the older men would suppress neural excitability of reflexes in the soleus muscle (SOL), as well as voluntarily and electrically induced ankle plantar flexor contractile properties, to a greater extent when compared with young men.

## 2. Materials and methods

### 2.1. Participants

Eleven young (19–21 years) and nine older (64–80 years) healthy subjects volunteered for the study. The physical characteristics of the subjects are presented in Table 1. All subjects were free of any known cardiovascular, respiratory, neurological, or metabolic diseases, and were not taking any related medications. All volunteers participated in recreational activities from two to four times per week and were considered physically active, without participating in any formal physical exercise or sports program. Written informed consent was obtained from all subjects after explaining all details of the experimental procedures and associated discomforts. All procedures were approved by the Regional Ethics Committee and were conducted according to the guidelines of the Declaration of Helsinki.

### 2.2. Experimental procedures

#### 2.2.1. Familiarization session

To attain a stable level of performance, at least 4 days before the visit to participate in experiments, participants attended

a familiarization session during which they were introduced to the experimental procedures for neuromuscular testing. During this session, each participant learned to achieve and maintain maximal-effort ankle plantar flexion for 3–4 s with a 250-ms stimulation train test at 100 Hz (TT-100 Hz) superimposed on a voluntary contraction, and their tolerance to electrical stimulation was assessed [34,35]. To control for circadian fluctuations in body temperature, all experiments began at 7:30 a.m. The experiment was performed at 23 °C ambient temperature and 55% relative humidity. Passive heating was conducted indoors at the same time of day (07:30 a.m. to 11:00 a.m.). Subjects had to sleep for >8 h the night before the experiment and to abstain from alcohol, and avoid heavy exercise and caffeine for no less than 24 h before the experiment. Aiming at evading the effect of diet-induced thermogenesis, the subjects did not eat from 12 h before the start of the experiment until it ended. To standardize the condition of hydration and the feeling of thirst, subjects were allowed to drink still water if they wanted until 60 min before the first body mass measurement [2,10,36,37].

#### 2.2.2. Experimental protocol

After arriving at the laboratory, the participants were asked to rest in a semirecumbent posture for 30 min dressed in a T-shirt, swimming shorts, and socks. Skin ( $T_{sk}$ ), muscle ( $T_{mu}$ ), and rectal ( $T_{re}$ ) temperature stabilization was established, and control  $T_{sk}$ ,  $T_{mu}$ , and  $T_{re}$  were measured. The participant was seated in the dynamometer chair with stimulating electrodes placed over the tibial nerve, electromyography electrodes—over the SOL of the right leg, and the reflexes were assessed. After a 2-min rest, when the electrodes were moved from over the tibial nerve to over the posterior calf muscle, the force-generating capacity of the posterior calf muscle was assessed by applying electrical stimuli at 1, 20, TT-100, and 100 Hz. The stimulation frequency was changed in about 3 s. After a 1-min rest, two attempts at a 3–4-s MVC with an interval of 1-min rest between them were performed applying a TT-100 Hz stimulus superimposed on the voluntary contraction [17,38]. Then, the participant began the water immersion heating protocol. The water bath temperature was approximately 43 °C and the participant was immersed to their waistline. Numerous epidemiological studies have indicated that the internal body (core) temperature is generally lower (by approximately 0.4 °C) in geriatric males (aged 65–95 years) than in younger adult men (aged 20–64 years) [39]. Considering this, the immersion continued until the  $T_{re}$  increased to 39.5 °C for the young group and to 39.0 °C for the older group, and the exposure time required to achieve this  $T_{re}$  was recorded.  $T_{re}$  were recorded throughout the heating procedure. Within 1 min of leaving the bath, the subject was towel-dried,  $T_{sk}$  and  $T_{mu}$  were measured. The volunteer was dressed in a long-sleeved sweater, trousers, socks, and a warm cap (balaclava). Then the neuromuscular testing was carried out in the same order as before the warm water immersion.

Table 1. Physical characteristics of the subjects.

	Young (n = 11)	Old (n = 9)
Age, years	21 ± 1	69 ± 6#
Height, cm	180.36 ± 1.92	176.6 ± 2.14
Mass, kg	78.22 ± 3.18	83.3 ± 5.23
Body surface area, m <sup>2</sup>	1.98 ± 0.04	2.00 ± 0.07
Mean subcutaneous fat, mm	10.64 ± 1.10	14.31 ± 1.18#
Body mass index, kg/m <sup>2</sup>	24.04 ± 0.87	26.47 ± 1.11#
Body fat, %	15.55 ± 1.19	24.89 ± 2.24#

Values are expressed as means and SEM.

# $p < .05$ , compared with young men.

## 2.3. Experimental measurements

### 2.3.1. Anthropometric measurements

The anthropometric characteristics of subjects are presented in Table 1. The participant's weight (kg), body fat (%), and height (in cm) were measured (TBF-300 body composition analyzer; Tanita, West Drayton, UK), and body mass index (BMI) was calculated. Body surface area (in  $m^2$ ) was estimated as  $128.1 \times \text{weight}^{0.44} \times \text{height}^{0.60}$  [40]. Skinfold thickness (in mm) was measured (SH5020 skinfold caliper; Saehan, Masan, Korea) at 10 sites (chin, subscapular, chest, side, supra ilium, abdomen, triceps, thigh, knee, and calf) and the mean subcutaneous fat thickness was calculated [41].

### 2.3.2. Body temperature measurements

Mouth or ear (tympanic) temperature is not a valid measure in respect to body core temperature [42].  $T_{re}$  has been criticized for its slow response to fluctuations in central blood temperature [43], while esophageal, stomach and tympanic membrane temperatures show faster response times [44–46], which means that  $T_{re}$  is less sensitive to external/surface temperature and is more a stable parameter in respect to other body parts, and its changes are dependent on central blood temperature rather than surface capillary temperature. Considering this,  $T_{re}$  was measured throughout the experimental trial using a rectal thermistor thermocouple sensor (Rectal Probe; Ellab, Hvidovre, Denmark; accuracy  $\pm 0.01$  °C) inserted to a depth of 12 cm past the anal sphincter. The rectal thermistor sensor was placed by the subject.  $T_{mu}$  and  $T_{sk}$  were measured before and at the end of the water immersion. The  $T_{mu}$  was measured with a needle microprobe (MKA; Ellab) inserted approximately 3.5 cm [47] under the skin covering the lateral gastrocnemius muscle of the right leg.  $T_{sk}$  was measured with thermistors taped at lateral gastrocnemius site (i.e. needle insertion site) (DM852; Ellab; accuracy  $\pm 0.01$  °C).

### 2.3.3. Torque-generating capacity measurement

The isometric torque of ankle plantar flexion muscles was assessed applying an isokinetic dynamometer (System 4; Biodex Medical Systems, Shirley, NY) calibrated according to the manufacturer's service manual with a correction for gravity performed using the Biodex Advantage program (version 4.X). Subjects were placed in the dynamometer chair with the trunk inclined at 45° with respect to the vertical, and with hip, knee, and ankle joint angulations of 90°, 100° (full knee extension = 180°), and 90°, respectively. To measure MVC (in Nm), the subject was asked to achieve and maintain maximal effort of ankle plantar flexion for 3–4 s. Each trace was examined visually to ensure that there were no artefactual spikes at the start of the signal curve. The subject's arms were crossed on their chest with the hands grasping the trunk-supporting belt during all tests on the dynamometer. Aiming at ensuring a maximal effort, standardized verbal encouragement was provided during each voluntary ankle plantar flexion trial by the same experienced researcher [17,48].

The subject positioning during the electrical stimulation assessment was essentially the same as that described above. The devices and procedure for electrically stimulated torque have been described previously [48]. In brief, muscle stimulation was applied using flexible surface electrodes (MARP Electronic, Krakow, Poland), covered with a thin layer of electrode gel (ECG Gel; Ceracarta, Forli, Italy), with one electrode (8 × 12 cm) placed transversely across the width of the proximal portion of the posterior calf just below the popliteal fossa, and the other electrode (8 × 8 cm) covered the distal portion of the muscle just below the fibers of the gastrocnemius muscle. A constant-current electrical stimulator (MG 440; Medicor, Budapest, Hungary) was used to deliver 0.5-ms square-wave pulses at 150 V. Peak torques (in Nm; measured from the baseline to the peak torque) induced by electrical stimulation at 1 Hz (P1; representing the properties of muscle excitation–contraction coupling), at 20 Hz (P20; representing the steep section of the force–frequency relationship curve), and at 100 Hz (P100; which is close to maximal force) were measured with a 3-s rest interval between electrical stimulations. The peak amplitude, contraction time (CT; in ms; the time interval from the beginning of a TT-100 Hz to the peak torque) and half-relaxation time (HRT; in ms; the time from the peak to half-maximum torque) were measured in resting TT-100 Hz (PTT100) contractions. A rest interval of 1 min was set between the electrical stimulation train and MVC measurements. During two attempts of 3–4-s MVC interspaced with a 1-min rest interval, PTT100 stimuli were superimposed on the approximately 3 s of MVC. The PTT100 contractions were used to assess the CAR of the posterior surae muscle. The CAR was calculated as described elsewhere [48] using following equation:  $CAR = MVC / (MVC + TT-100 \text{ Hz})$ , where a CAR of 1 indicates complete activation, whereas a CAR of less than 1 indicates central activation failure or inhibition.

### 2.3.4. Muscle activity-generating capacity

The subject positioning was essentially the same as that described above (see Section 2.3.3.). After careful preparation of the skin (shaving, abrading, and cleaning with alcohol wipes) to obtain low impedance, bipolar Ag–AgCl surface bar electrodes (10 mm diameter, 20 mm center-to-center distance) (DataLog type No. P3X8 USB; Biometrics, Gwent, UK) were used for electromyography activity (EMG) recording. For the SOL, the electrode was placed at 2/3 of the line between the medial condyle of the femur to the medial malleolus. The actual electrode position was marked with a waterproof marker, thereby the same recording site was used before and after low-body heating. The ground electrode was positioned on the tarsus of the same leg. EMG signals were recorded by amplifiers (gain 1000), with signal measurements using a third-order filter (18 dB/octave) bandwidth of 20–460 Hz. The analogue signal was sampled and converted to digital form at a sampling frequency of 5 kHz. The EMG signal was telemetered to a receiver that contained a differential amplifier with an input impedance of 10 M $\Omega$ , the input noise level was <5  $\mu$ V, and the common mode rejection ratio was higher than 96 dB. Before recording the EMG, we set the channel sensitivity at 3 V and excitation



output at 4600 mV as recommended by the manufacturer. EMG files were stored simultaneously on a biometrics memory card and PC hardware, and dedicated software (DataLog; Biometrics) was used for data processing and analysis. The EMG signal was converted to the root mean square (RMS, in mV), as a measure of EMG amplitude, and EMG mean frequency (MnF, in Hz) values for a 1000-ms epoch coinciding with 1-s force interval just before PTT100 were superimposed on MVCs [48].

### 2.3.5. Reflex recordings

SOL H-reflexes, V-waves, and M-waves were evoked by 0.5-ms square-wave pulses stimulated by a cathode placed in the popliteal cavity and an anode distal to the patella over the posterior tibial nerve with an interelectrode distance of about 4 cm. The resting maximal H-reflex ( $H_{max}$ ; which reflects motoneuron excitability, while also reflecting the efficiency of the transmission in Ia afferent motor-neuron synapses) and maximal M-wave ( $M_{max}$ ; which reflects sarcolemmal excitability) were obtained by increasing the electrical intensity by 3 V every 10 s in the 30–150 V range. With increasing stimulation intensity, the H-reflex response initially increased progressively before decreasing and then disappearing, whereas the M-wave achieved its maximum and remained stable. Thereafter, the subject was instructed to perform three brief MVCs of the plantar flexor muscles with at least a 1-min rest between contractions. A superimposed stimulus (at  $M_{max}$  intensity) was evoked to obtain the V-wave ( $V_{sup}$ ) [48]. The peak-to-peak amplitude of the V-wave reflects the magnitude of the central descending neural drive to spinal motor neurons, although spinal factors such as motor neuron excitability and pre- or postsynaptic inhibition may also be involved [49]. M-wave amplitude (in mV) was also used to normalize the amplitude of the recorded H-reflex wave (i.e.  $H_{max}/M_{max}$  ratio). This was done to ensure that any changes in the evoked  $H_{max}$  and  $V_{sup}$  amplitudes (in mV) were not induced by changes at the muscle fiber membrane or neuromuscular junction [16]. The latencies (in ms) of the electrically evoked action potentials were calculated from the stimulation artefact at the peak of the wave.

### 2.3.7. Statistical analysis

The normality of the data distribution was tested using the Kolmogorov–Smirnov test, and all data were found to be normally distributed. A mixed ANOVA was performed with one between-subjects factor (age: young vs. older) and time as within-subject factor (before vs. after heating) on the dependent variables (body temperatures and motor performance [reflexes, MVC, CAR, and RMS and MnF of the EMG of SOL muscle]). If significant interaction effect was found among factors, two-way mixed-design ANOVA using syntax with Bonferroni correction was performed to assess at which age group there is a time effect. A three-way mixed-design ANOVA using syntax with Bonferroni correction was performed to assess age and time effects at different stimulation conditions (electrically induced muscle properties). Comparisons for between-subjects factor at single time-point

were analyzed using independent-sample t tests on the subjects' baseline values (physical characteristics of participants) and on change values ( $\Delta$ ) from before to after lower-body heating. Statistical significance was defined as  $p < .05$ . Statistical analyses were performed using IBM SPSS Statistics software (v. 22; IBM Corp., Armonk, NY).

## 3. Results

The young and older men differed in average age by approximately 48 years ( $p < .05$ ) (Table 1). The older men had a higher percentage of body fat and mean subcutaneous fat ( $p < .05$ ). The two groups did not differ significantly in height, body mass, BMI, or body surface area ( $p > .05$ ).

### 3.1. Effects of Lower-Body heating on body temperatures

Baseline values for  $T_{re}$ , calf  $T_{mu}$ , and calf  $T_{sk}$  were lower in the older group than in the young group ( $p < .05$ ) (Table 2). In the young group, the time to warm the body from a  $T_{re}$  of  $37.07 \pm 0.08$  °C before warming to 39.5 °C was  $66.27 \pm 6.36$  min; in the older group, the time to warm the body from a  $T_{re}$  of  $36.59 \pm 0.09$  °C before warming to 39.0 °C was  $88.22 \pm 5.41$  min (age effect,  $p < .05$ ). Despite a similar  $T_{re}$  increase ( $2.41 \pm 0.09$  vs.  $2.46 \pm 0.08$ ;  $p > .05$ ) during the heating procedure in both group of men, calf  $T_{mu}$  ( $3.99 \pm 0.14$  vs.  $5.10 \pm 0.18$ ;  $p < .05$ ) and calf  $T_{sk}$  ( $7.65 \pm 0.33$  vs.  $9.92 \pm 0.62$ ;  $p < .05$ ) increased more in older men than in young men, respectively.

### 3.2. Effects of severe WBH on spinal and supraspinal reflex excitability

As can be seen in Figure 1, in healthy aged adults, we observed lower  $H_{max}$ ,  $V_{sup}$ , and  $M_{max}$  amplitude values, and lower  $H_{max}/M_{max}$  amplitude ratio (age effect,  $p < .05$ ). Severe WBH decreased  $H_{max}$  and  $V_{sup}$  amplitude (time effect,  $p < .05$ ) and this decrease was found to be similar in both groups of men (age effect,  $p > .05$ ). Under such hyperthermic conditions  $M_{max}$  amplitude was unaffected in both groups of men (time and age effect,  $p > .05$ ).

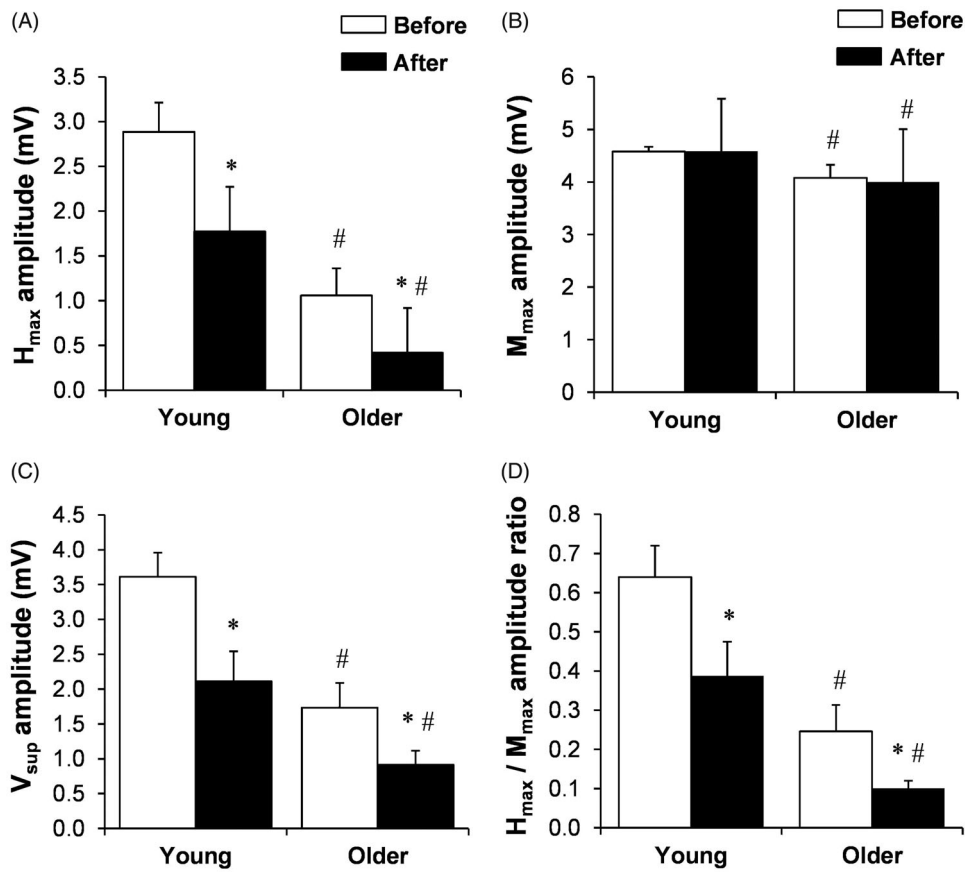
In the older men (vs. young men), the baseline latency time for  $H_{max}$  (Figure 2(A)) and  $V_{sup}$  (Figure 2(C)) was longer and for  $M_{max}$  (Figure 2(B)) was shorter (age effect,  $p < .05$ ). These reflex latencies decreased significantly after lower-body heating in both groups of men (time effect;  $p < .05$ ). Decrease in  $H_{max}$  and  $V_{sup}$  latencies from before to after heating ( $\Delta$ , in %) was found to be greater in older men than

Table 2. Body temperature before and after lower-body heating.

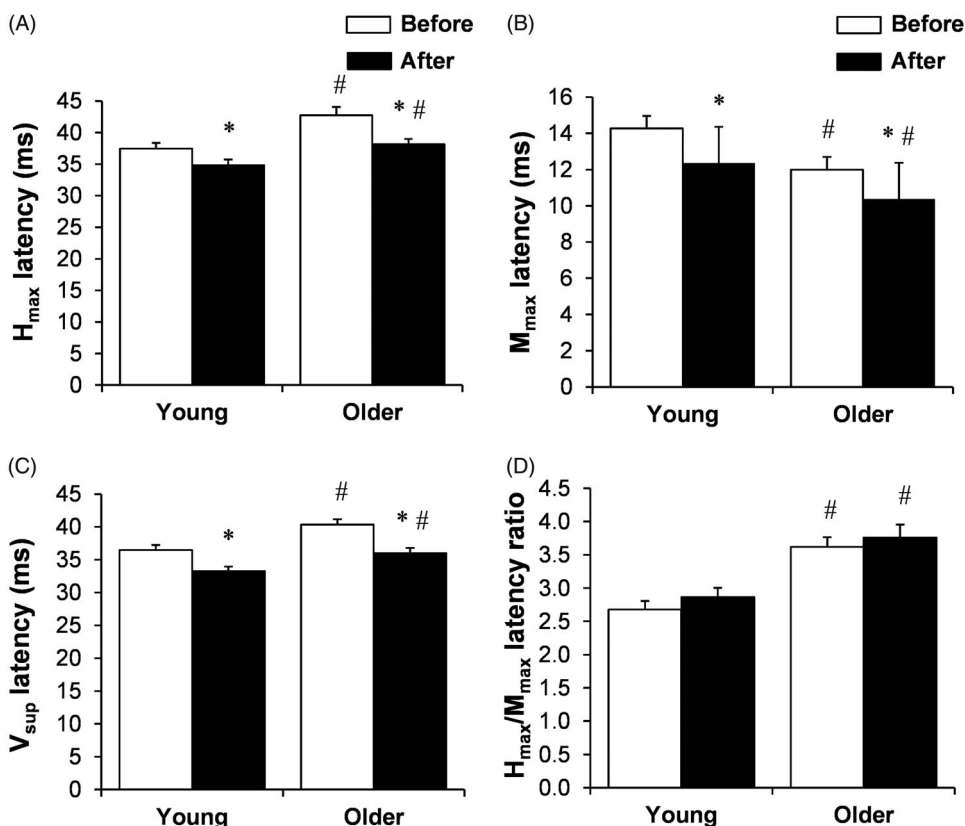
	Young		Old	
	Before	After	Before	After
Rectal T, °C	37.07 ± 0.08	39.5 (fixed)	36.59 ± 0.09#	39.0 (fixed)
Calf muscle T, °C	36.40 ± 0.09	40.39 ± 0.08*	35.07 ± 0.20#	40.17 ± 0.16*
Calf skin T, °C	31.82 ± 0.28	39.47 ± 0.14*	30.50 ± 0.39#	40.42 ± 0.31*#

\* $p < .05$  compared with before.

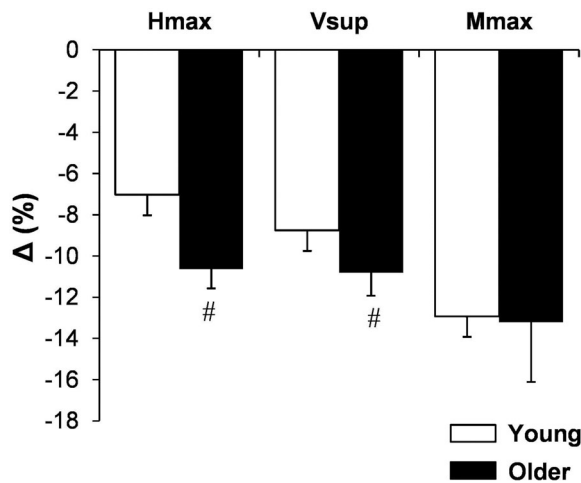
# $p < .05$  compared with young men. Values are expressed as means and SEM.



**Figure 1.** The reflex amplitude of  $H_{max}$  (A),  $M_{max}$  (B),  $V_{sup}$  (C), and  $H_{max}/M_{max}$  amplitude ratio (D) of soleus muscle in groups of young and older men before and after lower-body heating. \* $p < .05$ , compared with before; # $p < .05$ , compared with young men. Values are expressed as means and SEM.



**Figure 2.** The reflex latency of  $H_{max}$  (A),  $M_{max}$  (B),  $V_{sup}$  (C), and  $H_{max}/M_{max}$  latency ratio (D) of soleus muscle in groups of young and older men before and after lower-body heating. \* $p < .05$ , compared with before; # $p < .05$ , compared with young men. Values are expressed as means and SEM.



**Figure 3.** Lower-body heating induced change in  $H_{\max}$ ,  $V_{\text{sup}}$ , and  $M_{\max}$  reflex wave latency time in young and older men.  $\#p < .05$ , compared with young men, mean difference in percent between before and after lower-body heating. Values are expressed as means and SEM.

in young men (age effect,  $p < .05$ ) (Figure 3). Moreover,  $H_{\max}/M_{\max}$  latency ratio was greater in older men than in young men ( $p < .05$ ) (Figure 2(D)). However, there was no severe WBH effect on age-related changes in  $H_{\max}/M_{\max}$  latency ratio ( $p > .05$ ).

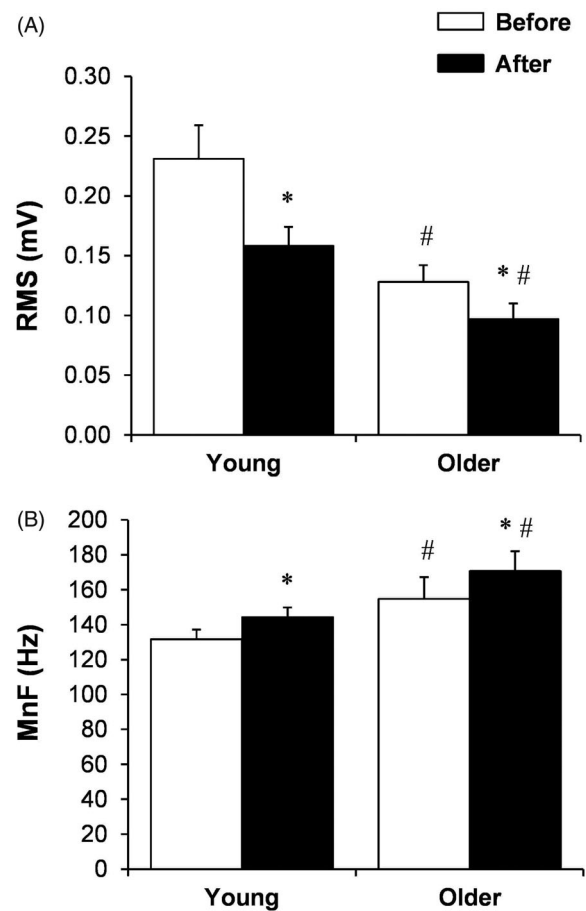
### 3.3. Effects of severe WBH on skeletal muscle EMG

In healthy aged adults, we observed lower SOL RMS (Figure 4(A)) and greater SOL MnF (Figure 4(B)) responses of the surface EMG signal during brief MVC (age effect,  $p < .05$ ). Severe WBH decreased SOL RMS and increased SOL MnF similarly in both groups of men (time effect,  $p < .05$ ; age effect,  $p > .05$ ).

### 3.4. Effects of severe WBH on Torque-Generating capacity

At baseline, regardless of voluntarily (MVC; Figure 5(C)) or electrically induced (P1, P20, PTT100 and P100; Figure 5(B)) plantarflexion muscle contractions, older men produced significantly less torque than young men. The data also indicated a slowing of the contractile and relaxation muscle kinetics in older men (vs. young men), as indicated by the PTT100 induced muscle contraction (Figure 5(D)) and half-relaxation (Figure 5(E)) times. The CAR of the plantarflexion muscles, tested by the superimposed stimulation method, appeared to be maximal or near maximal in both young and older subjects (Figure 5(F)).

In the older men (vs. young men), greater increase in  $T_{\text{mu}}$  induced by lower-body heating (Table 2) was accompanied with a significant increase in P1 and PTT100 torque (age and time effect,  $p < .05$ ) (Figure 5(B)). Interestingly, this change in torque was also accompanied by a greater decrease ( $\Delta$ , in %) in muscle CT (faster contraction) ( $-8.38 \pm 1.81\%$  vs.  $-13.86 \pm 1.57\%$  in young and older men, respectively;  $p < .05$ ); whereas HRT decreased ( $\Delta$ , in %) similarly in both groups of men (time effect,  $p < .05$ ; age effect,  $p > .05$ ). Severe WBH did not impair voluntary activation (CAR) of

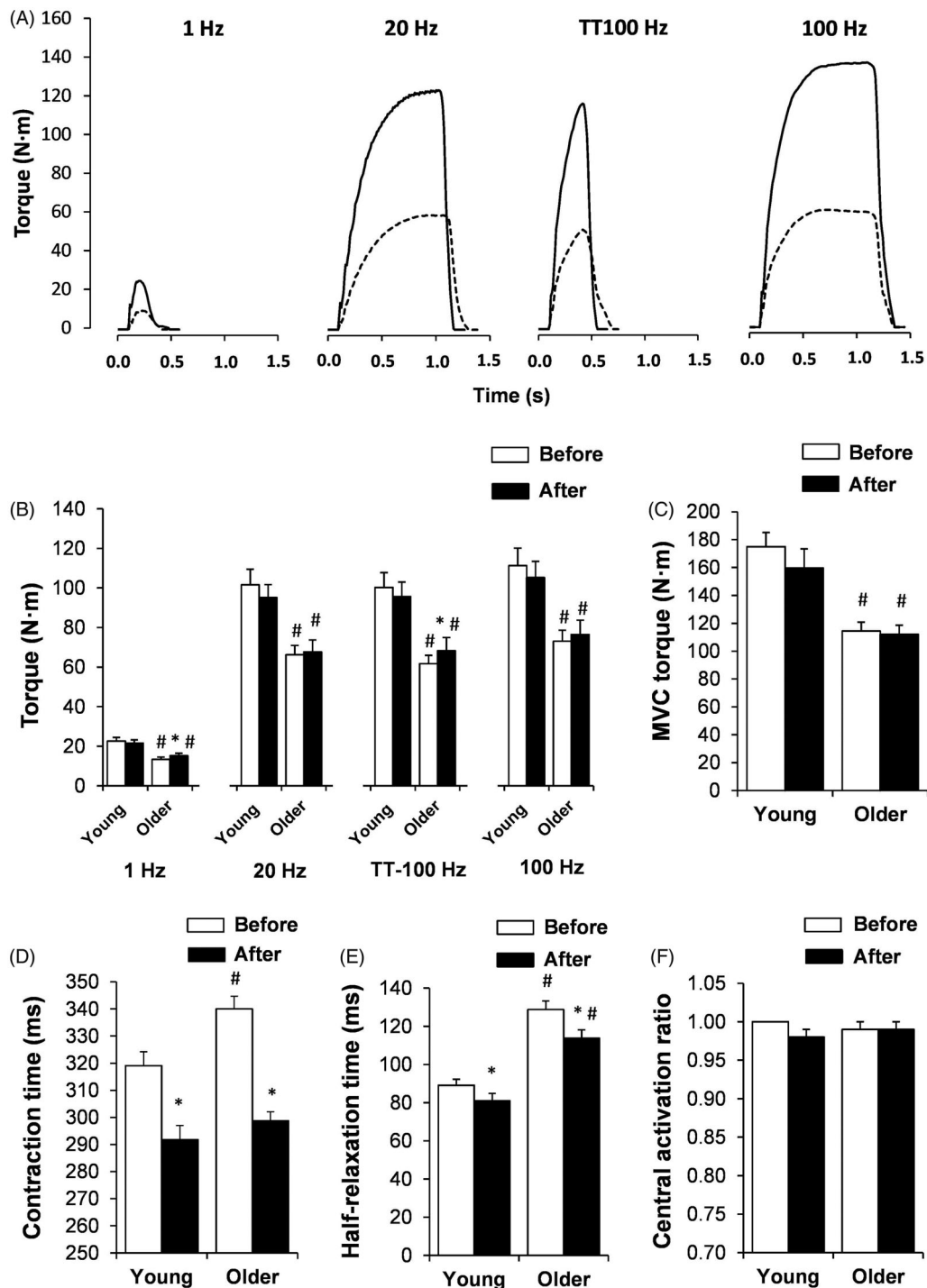


**Figure 4.** The root mean square (RMS) values (A) and mean frequency (MnF) values (B) of the surface EMG signal of soleus muscle during the 5-s MVC before and after lower-body heating in groups of young and older men.  $*p < .05$ , compared with before;  $\#p < .05$ , compared with young men. Values are expressed as means and SEM.

exercising muscles during the brief 5-s MVC in both groups of men ( $p > .05$ ).

## 4. Discussion

To our knowledge, this study is the first to investigate the effects of severe WBH (increase in  $T_{\text{re}}$  of approximately  $2.5^\circ\text{C}$  from baseline) on neuromuscular function in healthy young and older men. A unique finding of our study is that, in older men (vs. young men), severe WBH induces greater decrease ( $\Delta$ ) in latency (faster response) only for spinal ( $H_{\max}$ ) and supraspinal ( $V_{\text{sup}}$ ) excitability in the transmission of the neural drive, whereas no aging affect was found for the decrease ( $\Delta$ ) in reflex amplitude. These observed age-related differences in reflex excitability did not affect the change ( $\Delta$ ) in SOL surface EMG signal components (RMS, amplitude and MnF, frequency) during brief MVC performed in normothermic and hyperthermic conditions. In older men, greater increase in calf  $T_{\text{mu}}$  with respect to  $T_{\text{re}}$  during lower-body heating, than in young men, was accompanied by a significant increase in P1 and PTT100 torque in parallel with a greater decrease in muscle CT indicated by the TT100-induced muscle contraction. In the present study, age-related changes in motor drive and muscle contractility affected by



**Figure 5.** Representative torque records (A) of electrically stimulated contractions at 1, 20, TT-100, and 100 Hz in ankle plantar flexion muscles of a young (solid lines) and older (dashed lines) men obtained in thermoneutral conditions (i.e. before lower-body heating). The electrically induced ankle plantar flexion muscle isometric torque by stimuli at 1, 20, TT-100, and 100 Hz (B), maximal voluntary contraction (MVC) torque (C), contraction time (D) and half-relaxation time (E) indicated by the PTT100-induced muscle contraction, and central activation ratio, (F) before and after passive lower-body heating in groups of young and older men. \* $p < .05$ , compared with before; # $p < .05$ , compared with young men. Values are expressed as means and SEM.

severe WBH do not affect the change in brief MVC torque production or central activation differently between young and older men.

Our present study results confirm the progressive age-related impairment of the neural drive at the peripheral and spinal level in a thermoneutral condition. Various mechanisms, affecting afferent and efferent pathways, as well as interneurons (modified presynaptic inhibition), may be

responsible for the aged-related decrease in reflex responses [22,50]. Functionally, delayed spinal reflex loop (determined by H-reflex latency) potentially contributes to postural instability and greater falls in older adults [51,52]. Longer H- and V-wave latency exhibited by our older subjects seems likely to be consistent with a neural structural remodeling hypothesis, including drop-out of the largest fibers, and a segmental demyelination and remyelination process, with a



consequent reduction in the density of unmyelinated and myelinated neurons [5,53]. Furthermore, because the longer reflex latency in older men (vs. young men) was accompanied by shorter direct motor contractile time ( $H_{\max}/M_{\max}$  latency ratio; Figure 2(D)) it seems indicative that sensory fibers are affected before motor fibers with aging, as previously observed [21,22]. In view of the progressive slowing of motor conduction velocity with aging, the improvements of the  $M_{\max}$  latency observed in our present study appears as an unexpected result, and thus seems to affect the fast-conducting nerve fibers preferentially [5]. Nevertheless, the aim of our study was to examine whether severe WBH in the older men would suppress excitability of reflexes in SOL to a greater extent compared with that in the young men. We here expected that mainly because of essential age-related alterations at the afferent level [21,22] in line with spinal modulation of neural drive, which relates partly to presynaptic inhibition mediated by temperature-sensitive groups III and IV afferents [18–20], spinal modulation of neural drive is likely to be suppressed more by severe WBH in older men than in young men. By contrast with our expectation, we observed that spinal and supraspinal excitability during severe WBH was preserved in older age. Resting core, skin, and muscle temperature were notably lower in our older men than in young men, which makes it possible to suggest that motor drive in older men during daily activities operates at slower rates not only because of age-related decline in neuromuscular structural and functional properties, as suggested previously [21,22], but also because of lower resting body temperature. In view of the attenuated heat transfer and loss during lower-body heating with age, more heat was stored in the calf muscle and calf skin of the older men than in the young men. As a result, we showed a greater increase in afferent axon potential conduction velocity ( $H_{\max}$  and  $V_{\text{sup}}$  latency) in hyperthermic older men than in young men, which gives an indication of temperature-dose-dependent acceleration in opening and closing of  $\text{Na}^+$  channels in nerve and muscle membranes [54]. Considering that in aged nerves there could be an acquiring  $\text{Na}^+$  channelopathy, with ectopic expression of  $\text{NaV1.8}$  isoform on motor axons [23], the activity of which is related to temperature (e.g. hyperthermia) [24,25] may serve as a possible explanation by suggesting that observed changes in temperature unmask changes in axonal excitability with aging. These findings imply age-related temperature-dependent modification of conduction velocity of Ia afferents or an increase synaptic transmission efficacy [55]. Thus, in our present study, age-related modification of neural excitability does not significantly affect voluntary activation (CAR) of exercising muscle during a brief 5-s MVC torque production under either normothermic or hyperthermic conditions.

Under thermoneutral conditions, the ankle plantar flexor contractile properties of the older men in our present study showed the typical traits of senile muscle (reduced torque and slower contraction kinetics) in accordance with data from previous studies [22,56,57]. The novel contribution of the present study was the use of lower-body heating that induced severe WBH, under which our analysis points to an

absence of modification in muscle contractile properties with age. We showed a greater decrease in muscle CT (faster contraction) and significant increase in P1 and PTT100 torque production response to severe WBH in older men than in young men. These present results indirectly suggest age-related temperature-dependent oxidative shift to milder oxidation specifically leading to increased myofibrillar  $\text{Ca}^{2+}$  sensitivity in fast-twitch skeletal muscle fibers [29], whereas temperature-dependent increase in myofibrillar  $\text{Ca}^{2+}$  sensitivity is highly likely because of augmented  $\text{Ca}^{2+}$  binding to the troponin complex [58]. However, under such experimental conditions tetanic torque induced by low (20 Hz; 1000 ms) and high (100 Hz; 1000 ms) frequencies was not affected in either group of men, which suggests no age-related temperature-dependent effect on changes in the ability of cross-bridges to generate force or changes in the intracellular calcium (availability) during tetani (tetanic  $[\text{Ca}^{2+}]_i$ ) [29,59,60]. Our present finding appears analogous to that of a study of intact mouse muscle fibers, in which no change in tetanic (100 Hz, 600 ms) force in soleus fibers was found when the temperature was increased from 37 to 43 °C [60]. In addition, the brief 5-s MVC torque production was not affected by severe WBH in either group of men.

Taken together, the findings of our present study suggest that motor performance was preserved in severe WBH with advanced healthy aging. Furthermore, our results suggest that in older men (vs. young men) greater increase in afferent conduction velocity and an increase synaptic transmission efficacy (faster H-reflex loop) consistent with greater increase in electrically induced muscle torque development (faster muscle contraction) may contribute to potential age-related motor drive modification to facilitate motor (central and peripheral) performance with respect to high body temperatures. From a functional point of view, as the body warms-up, the potentiated neural excitability associated with a greater torque development may be regarded as a way to increase the ability to maintain an upright posture during sudden balance perturbation in aged men.

#### 4.1. Limitations

The present study has some limitations. For middle-aged and older adults with chronic medical conditions (e.g. type 2 diabetes, pulmonary disease, and cardiovascular disease) or lower levels of aerobic fitness, the risk of heat-related injury may be greater [61] than that in the older men recruited for the purposes of the present study, who were active, healthy, and free of any known medical conditions. This suggests that a limitation of the present study is that its results probably cannot be universally applied to older people with the aforementioned physiological conditions. Moreover, as compared with young adults (21–29 years of age), older adults (63–80 years of age) showed that sensory nerve fibers are affected before motor fibers with aging. By contrast, the oldest group of adults (>80 years old) demonstrated global declines in both motor and sensory nerve conduction velocities and response amplitudes [21], suggesting that the results of the present study may not be directly applicable to

very old healthy adults. Older individuals are the most vulnerable population during prolonged environmental heat exposure, and experience significantly worse health outcomes than any other age group [62]. In the present study, we induced acute short-term severe WBH in groups of young and older men; therefore, the results of any study involving short-term severe WBH should be interpreted cautiously with respect to the situations of prolonged hyperthermia (e.g. climactic heat wave).

## 5. Conclusion

We examined whether severe whole-body hyperthermia suppresses neuromuscular (central and peripheral) functions in older men more than in young men. Our primary finding was that despite delayed and weakened thermoregulation [2], and age-related decline in neuromuscular function, healthy aging preserved motor performance in severe whole-body hyperthermia. Aging shows an even greater lower-body heating-induced increase in potentiation of the muscle torque development and spinal reflex loop conduction velocity. We have offered a possible explanation for our findings, but further research is needed to draw firm conclusions, especially regarding the whole-body hyperthermia effects in aged people on motor performance for posture control and mobility (motor control), and resistance to fatigue induced by prolonged or complex exercise tasks that are more suitable for real-life (field) situations (e.g. firefighters, or when exercising in a hot environment).

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## References

- [1] Hunter SK, Pereira HM, Keenan KG. The aging neuromuscular system and motor performance. *J Appl Physiol.* 2016;121:982–995.
- [2] Brazaitis M, Paulauskas H, Eimantas N, et al. Heat transfer and loss by whole-body hyperthermia during severe lower-body heating are impaired in healthy older men. *Exp Gerontol.* 2017;96:12–18.
- [3] Rolland Y, Czerwinski S, Van Kan GA, et al. Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. *J Nutr Health Aging.* 2008;12:433–450.
- [4] Vijg J, Campisi J. Puzzles, promises and a cure for ageing. *Nature.* 2008;454:1065–1071.
- [5] Wang FC, de Pasqua V, Delwaide PJ. Age-related changes in fastest and slowest conducting axons of thenar motor units. *Muscle Nerve.* 1999;22:1022–1029.
- [6] Metter EJ, Talbot LA, Schrager M, et al. Skeletal muscle strength as a predictor of all-cause mortality in healthy men. *J Gerontol A Biol Sci Med Sci.* 2002;57:B359–B365.
- [7] Marzetti E, Leeuwenburgh C. Skeletal muscle apoptosis, sarcopenia and frailty at old age. *Exp Gerontol.* 2006;41:1234–1238.
- [8] Inoue Y, Nakao M, Araki T, et al. Regional differences in the sweating responses of older and younger men. *J Appl Physiol.* 1991;71:2453–2459.
- [9] Larose J, Wright HE, Stapleton J, et al. Whole body heat loss is reduced in older males during short bouts of intermittent exercise. *Am J Physiol Regul Integr Comp Physiol.* 2013;305:R619–R629.
- [10] Inoue Y, Shibasaki M, Hirata K, et al. Relationship between skin blood flow and sweating rate, and age related regional differences. *Eur J Appl Physiol Occup Physiol.* 1998;79:17–23.
- [11] Gagnon D, Romero SA, Ngo H, et al. Healthy aging does not compromise the augmentation of cardiac function during heat stress. *J Appl Physiol.* 2016;121:885–892.
- [12] Romero SA, Gagnon D, Adams AN, et al. Acute limb heating improves macro- and microvascular dilator function in the leg of aged humans. *Am J Physiol Heart Circ Physiol.* 2017;312:H89–H97.
- [13] Guergova S, Dufour A. Thermal sensitivity in the elderly: a review. *Ageing Res Rev.* 2011;10:80–92.
- [14] Schlader ZJ, Gagnon D, Adams A, et al. Cognitive and perceptual responses during passive heat stress in younger and older adults. *Am J Physiol Regul Integr Comp Physiol.* 2015;308:R847–R854.
- [15] Bain AR, Nybo L, Ainslie PN. Cerebral vascular control and metabolism in heat stress. *Compr Physiol.* 2015;5:1345–1380.
- [16] Racinais S, Gaoua N, Grantham J. Hyperthermia impairs short-term memory and peripheral motor drive transmission. *J Physiol.* 2008;586:4751–4762.
- [17] Brazaitis M, Eimantas N, Daniuseviciute L, et al. Two strategies for the acute response to cold exposure but one strategy for the response to heat stress. *Int J Hyperthermia.* 2015;31:325–335.
- [18] Bigland-Ritchie BR, Dawson NJ, Johansson RS, et al. Reflex origin for the slowing of motoneurone firing rates in fatigue of human voluntary contractions. *J Physiol.* 1986;379:451–459.
- [19] Duchateau J, Balestra C, Carpentier A, et al. Reflex regulation during sustained and intermittent submaximal contractions in humans. *J Physiol.* 2002;541:959–967.
- [20] Avela J, Finni J, Komi PV. Excitability of the soleus reflex arc during intensive stretch–shortening cycle exercise in two power-trained athlete groups. *Eur J Appl Physiol.* 2006;97:486–493.
- [21] Bouche P, Cattelin F, Saint-Jean O, et al. Clinical and electrophysiological study of the peripheral nervous system in the elderly. *J Neurol.* 1993;240:263–268.
- [22] Scaglioni G, Narici MV, Maffiuletti NA, et al. Effect of ageing on the electrical and mechanical properties of human soleus motor units activated by the H reflex and M wave. *J Physiol.* 2003;548:649–661.
- [23] Moldovan M, Rosberg MR, Alvarez S, et al. Aging-associated changes in motor axon voltage-gated Na<sup>+</sup> channel function in mice. *Neurobiol Aging.* 2016;39:128–139.
- [24] Zimmermann K, Leffler A, Babes A, et al. Sensory neuron sodium channel Nav1.8 is essential for pain at low temperatures. *Nature.* 2007;447:856–859.
- [25] Howells J, Czesnik D, Trevillion L, et al. Excitability and the safety margin in human axons during hyperthermia. *J Physiol.* 2013;591:3063–3080.
- [26] Hunter SK, Thompson MW, Ruell PA, et al. Human skeletal sarcoplasmic reticulum Ca<sup>2+</sup> uptake and muscle function with aging and strength training. *J Appl Physiol.* 1999;86:1858–1865.

- [27] Jiménez-Moreno R, Wang Z-M, Gerring RC, et al. Sarcoplasmic reticulum Ca<sup>2+</sup> release declines in muscle fibers from aging mice. *Biophys J*. 2008;94:3178–3188.
- [28] Miller MS, Bedrin NG, Callahan DM, et al. Age-related slowing of myosin actin cross-bridge kinetics is sex specific and predicts decrements in whole skeletal muscle performance in humans. *J Appl Physiol*. 2013;115:1004–1014.
- [29] Lamboley CR, Wyckelsma VL, Dutka TL, et al. Contractile properties and sarcoplasmic reticulum calcium content in type I and type II skeletal muscle fibres in active aged humans. *J Physiol*. 2015;593:2499–2514.
- [30] Durham WJ, Aracena-Parks P, Long C, et al. RyR1 S-nitrosylation underlies environmental heat stroke and sudden death in Y522S RyR1 knockin mice. *Cell*. 2008;133:53–65.
- [31] Bellinger AM, Reiken S, Carlson C, et al. Hypernitrosylated ryanodine receptor calcium release channels are leaky in dystrophic muscle. *Nat Med*. 2009;15:325–330.
- [32] Andersson DC, Betzenhauser MJ, Reiken S, et al. Ryanodine receptor oxidation causes intracellular calcium leak and muscle weakness in aging. *Cell Metab*. 2011;14:196–207.
- [33] Zuo L, Christofi FL, Wright VP, et al. Intra- and extracellular measurement of reactive oxygen species produced during heat stress in diaphragm muscle. *Am J Physiol Cell Physiol*. 2000;279:C1058–C1066.
- [34] Bernecke V, Pukenas K, Imbrasienė D, et al. Test-retest cross-reliability of tests to assess neuromuscular function as a multidimensional concept. *J Strength Cond Res*. 2015;29:1972–1984.
- [35] Kyguoliene L, Skurvydas A, Eimantas N, et al. Effect of constant, predictable, and unpredictable motor tasks on motor performance and blood markers of stress. *Exp Brain Res*. 2017;235:1323–1336.
- [36] Larose J, Boulay P, Wright-Beatty HE, et al. Age-related differences in heat loss capacity occur under both dry and humid heat stress conditions. *J Appl Physiol*. 2014;117:69–79.
- [37] Pranskunas A, Pranskuniene Z, Milieskaite E, et al. Effects of whole body heat stress on sublingual microcirculation in healthy humans. *Eur J Appl Physiol*. 2015;115:157–165.
- [38] Brazaitis M, Eimantas N, Daniuseviciute L, et al. Two strategies for response to 14 °C cold-water immersion: is there a difference in the response of motor, cognitive, immune and stress markers?. *PLoS One*. 2014;9:e109020–e109020.
- [39] Blatteis CM. Age-dependent changes in temperature regulation – a mini review. *Gerontology*. 2012;58:289–295.
- [40] Tikuisis P, Meunier P, Jubenville C. Human body surface area: measurement and prediction using three dimensional body scans. *Eur J Appl Physiol*. 2001;85:264–271.
- [41] McArdle W, Magel J, Gergley T, et al. Thermal adjustment to cold-water exposure in resting men and women. *J Appl Physiol*. 1984;56:1565–1571.
- [42] Hayward JS, Eckerson JD, Kemna D. Thermal and cardiovascular changes during three methods of resuscitation from mild hypothermia. *Resuscitation*. 1984;11:21–33.
- [43] Gagnon D, Lemire BB, Jay O, et al. Aural canal, esophageal, and rectal temperatures during exertional heat stress and the subsequent recovery period. *J Athletic Train*. 2010;45:157–163.
- [44] Molnar GW, Read RC. Studies during open-heart surgery on the special characteristics of rectal temperature. *J Appl Physiol*. 1974;36:333–336.
- [45] Kolka MA, Quigley MD, Blanchard LA, et al. Validation of a temperature telemetry system during moderate and strenuous exercise. *J Therm Biol*. 1993;18:203–210.
- [46] Shiraki K, Konda N, Sagawa S. Esophageal and tympanic temperature responses to core blood temperature changes during hyperthermia. *J Appl Physiol*. 1986;61:98–102.
- [47] Brazaitis M, Skurvydas A, Vadopalas K, et al. Force variability depends on core and muscle temperature. *J Therm Biol*. 2010;35:386–391.
- [48] Brazaitis M, Paulauskas H, Skurvydas A, et al. Brief rewarming blunts hypothermia-induced alterations in sensation, motor drive and cognition. *Front Physiol*. 2016;7:592.
- [49] Aagaard P, Simonsen EB, Andersen JL, et al. Neural adaptation to resistance training: changes in evoked V-wave and H-reflex responses. *J Appl Physiol*. 2002;92:2309–2318.
- [50] Morita H, Shindo M, Yanagawa S, et al. Progressive decrease in heteronymous monosynaptic Ia facilitation with human ageing. *Exp Brain Res*. 1995;104:167–170.
- [51] Kocejka DM, Mynark RG. Comparison of heteronymous monosynaptic Ia facilitation in young and elderly subjects in supine and standing positions. *Int J Neurosci*. 2000;104:1–15.
- [52] Shaffer SW, Harrison AL. Aging of the somatosensory system: a translational perspective. *Phys Ther*. 2007;87:193–207.
- [53] Jacobs JM, Love S. Qualitative and quantitative morphology of human sural nerve at different ages. *Brain*. 1985;108: 897–924.
- [54] Hodgkin A, Katz B. The effect of temperature on the electrical activity of the giant axon of the squid. *J Physiol*. 1949;109:240.
- [55] Scaglioni G, Ferri A, Minetti AE, et al. Plantar flexor activation capacity and H reflex in older adults: adaptations to strength training. *J Appl Physiol*. 2002;92:2292–2302.
- [56] Vandervoort AA, Hayes KC. Plantarflexor muscle function in young and elderly women. *Europ J Appl Physiol*. 1989;58:389–394.
- [57] Winegard KJ, Hicks AL, Vandervoort AA. An evaluation of the length–tension relationship in elderly human plantarflexor muscles. *J Gerontol A Biol Sci Med Sci*. 1997;52A: B337–B343.
- [58] Hwee DT, Cheng AJ, Hartman JJ, et al. The Ca<sup>2+</sup> sensitizer CK-2066260 increases myofibrillar Ca<sup>2+</sup> sensitivity and submaximal force selectively in fast skeletal muscle. *J Physiol*. 2017;595:1657–1670.
- [59] Westerblad H, Allen DG. Changes of myoplasmic calcium concentration during fatigue in single mouse muscle fibers. *J Gen Physiol*. 1991;98:615–635.
- [60] Place N, Yamada T, Zhang SJ, et al. High temperature does not alter fatigability in intact mouse skeletal muscle fibres. *J Physiol*. 2009;587:4717–4724.
- [61] Kenny GP, Yardley J, Brown C, et al. Heat stress in older individuals and patients with common chronic diseases. *Can Med Assoc J*. 2010;182:1053–1060.
- [62] Kenney WL, Craighead DH, Alexander LM. Heat waves, aging, and human cardiovascular health. *Med Sci Sports Exerc*. 2014;46:1891–1899.