ORIGINAL RESEARCH

Effect of Caffeine Intake on Finger Cold-Induced Vasodilation

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Objective.—The purpose of the study was to investigate the effect of caffeine intake on finger cold-induced vasodilation (CIVD).

Methods.—Ten healthy men underwent 6 experimental trials characterized by control (NCAFF) or caffeine intake (CAFF) via chewing gum (300 mg of caffeine) while resting on a chair or performing submaximal (70% maximal oxygen consumption) or maximal (100% maximal oxygen consumption) treadmill exercise (Bruce protocol) followed by immersion of the middle finger in a water bath (5°C) for 20 minutes. Finger temperature (T_f) and time parameters of the first CIVD cycle and post-test norepinephrine were measured.

Results.—Exercise duration for submaximal and maximal exercise was 8.9 ± 0.9 and 12.4 ± 0.8 minutes, respectively. CAFF had no effect on T_f , but exercise increased minimal T_f in NCAFF ($9.08 \pm 1.27^\circ\text{C}$, $13.02 \pm 2.13^\circ\text{C}$, and $13.25 \pm 1.63^\circ\text{C}$ in rest, submaximal, and maximal exercise, respectively) and CAFF ($8.76 \pm 1.39^\circ\text{C}$, $12.50 \pm 1.91^\circ\text{C}$, and $12.79 \pm 1.20^\circ\text{C}$). Maximal T_f was significantly higher in NCAFF ($15.98 \pm 1.04^\circ\text{C}$, $16.18 \pm 1.56^\circ\text{C}$, and $15.14 \pm 1.52^\circ\text{C}$) than in CAFF ($13.56 \pm 1.19^\circ\text{C}$, $15.52 \pm 1.31^\circ\text{C}$, and $14.39 \pm 1.43^\circ\text{C}$), resulting in a significant difference between minimal and maximal T_f in rest (NCAFF, $6.89 \pm 1.56^\circ\text{C}$ and CAFF, $4.79 \pm 1.23^\circ\text{C}$), but not in exercise conditions. CAFF had no effect on CIVD time responses, but exercise significantly shortened CIVD onset and peak time compared with rest in both NCAFF and CAFF. Norepinephrine concentration was significantly greater in CAFF (290.6 ± 113.0 pg/mL, 278.1 ± 91.4 pg/mL, and 399.8 ± 125.5 pg/mL) than NCAFF (105.6 ± 29.5 pg/mL, 199.6 ± 89.6 pg/mL, and 361.5 ± 171.3 pg/mL).

Conclusions.—Caffeine intake before finger immersion in cold water does not result in a thermogenic effect and adversely affects CIVD responses, whereas exercise modifies CIVD temperature and time responses.

Key words: cold exposure, peripheral blood flow, body temperature, vasoconstriction, norepinephrine

Introduction

Cold stress is a common environmental challenge encountered by individuals in recreational (eg, mountaineering, scuba diving) and occupational (eg, fishing industry) settings, and cold-induced health problems such as hypothermia and frostbite are of interest in wilderness medicine. Physiologically, cold exposure evokes thermoregulatory adjustments to maintain normal

body temperature. Specifically, cutaneous vasoconstriction via α -adrenergic receptor activation rapidly occurs, leading to a reduction in blood flow to the skin and subsequent lower skin temperature, but consequently the vasoconstriction decreases heat loss as a result of a decrement in the thermal gradient between the skin surface and surrounding environment.^{1,2} This reduced blood flow to peripheral regions of the body (eg, finger, toe) is paradoxically reversed by vasodilation, termed cold-induced vasodilation (CIVD), approximately 5 to 10 minutes after cold exposure, as first identified by Lewis.³ Although causative and regulatory mechanisms of CIVD remain unsolved (see reviews by Daanen⁴ and Cheung and Daanen⁵ for proposed mechanisms of

Prior presentation: Presented at the annual meeting of the American College of Sports Medicine, San Francisco, CA, May 28–June 1, 2012.

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CIVD), this phenomenon is thought to protect the periphery from cold injuries such as frostbite,^{6,7} but is often absent or affected by variable factors such as age, physical fitness, and cold acclimatization.⁴ A recent study by Cheung and Daanen,⁵ who delineated the trainability of CIVD via microcirculatory adaptations to repeated cold exposure, concluded that physiological improvement in CIVD is “neither guaranteed nor predictable,” despite equivocal results from both field and laboratory studies of CIVD. Thus, there is still a need for investigations extending the literature of CIVD.

Caffeine is widely present in the diet of the general population and also has long drawn attention to its ergogenic potential for athletic performance. Published evidence has shown that caffeine intake improves endurance performance⁸ and maximal voluntary contraction strength,⁹ although mechanisms for its ergogenic effects are still equivocal. From thermoregulatory perspectives, caffeine, specifically trimethylxanthine, has been shown to increase the metabolic rate (greater heat production)¹⁰ and reduce cutaneous blood flow (less heat dissipation)¹¹ during rest in thermoneutral environments. However, other studies report that caffeine does not induce added thermogenic effects¹² or affect cutaneous blood flow¹³ during exercise in the heat. Similarly, the thermogenic effect of caffeine on maintaining body temperature during whole body cold exposure is inconclusive among previous studies,^{14–17} whereas enhanced plasma free fatty acid mobilization and catecholamine stimulation,⁷ either singly or in combination, have been speculated to contribute to the caffeine-induced elevation in thermogenesis.^{14,16,18}

From a behavioral perspective, it is not uncommon to observe individuals who prepare for, or are about to engage in, outdoor activities in the cold to ingest a hot drink containing caffeine, such as coffee or tea, in an effort to warm up the body actually or perceptually. Apart from the previously conflicting observations on added thermogenic effects, whether caffeine intake affects CIVD response to cold would provide useful information in wilderness medicine concerning local cold injuries. To our knowledge, no study has yet investigated the effects of caffeine on the peripheral CIVD responses while exposed to cold environments, although this is a very probable scenario in daily life. Thus, the purpose of the present study was to investigate how caffeine intake before cold exposure influences CIVD responses in the immersed finger during rest and after exercise. We hypothesized that caffeine intake before cold exposure would not induce elevated temperature responses of CIVD in the immersed finger.

Methods

SUBJECTS

Ten healthy male college students were recruited for the present study. Specific exclusion criteria included habitual caffeine use (eg, coffee, tea, or energy drinks), positive histories for cardiovascular or metabolic disease, cold injuries (eg, frostbite), or current use of any medication (eg, antihypertensive) that might affect peripheral microcirculation and, thus, CIVD responses. All subjects provided a health-screening questionnaire and underwent a graded exercise test to identify a possible limitation to performing the present exercise protocol. The study subjects' physical characteristics are summarized in the [Table](#). They were then given an orientation session for experimental procedures and risks associated with study participation before obtaining written informed consent. The present study was reviewed and approved by the Protocol Review Committee of the College of Physical Education, Kookmin University, and conformed to the Declaration of Helsinki.

PROCEDURE

Subjects reported to the laboratory at 08:30 AM while instructed to abstain from a meal for 3 hours and strenuous exercise and alcohol consumption for at least 24 hours, as these behavioral variables have been reported to significantly influence finger blood flow response during cold exposure.^{19–21} Each experimental trial was separated by at least 48 hours to allow for full recovery from the prior study participation.

In all trials, on arrival at the laboratory, the subjects provided a midstream urine sample to determine their hydration status using a urine specific gravity (USG) refractometer (Model-UG1, Atago, Japan). They were dressed in comfortable sportswear and were instrumented with measurement sensors before participating in 6 experimental trials differentiated by caffeine intake (no caffeine vs caffeine) and exercise state (rest, submaximal, or maximal exercise), in random order. Subjects then rested quietly on a chair for 30 minutes in a room maintained at 27°C and 50% to 60% relative humidity, as these environmental conditions have been suggested to attain a better reproducibility of CIVD responses.⁴ During this stabilization period, baseline core temperature (T_{re}) and heart rate (HR) were monitored to ensure that the participants achieved a complete resting state. After the baseline measurements, the subjects immersed the middle finger for 5 minutes in a 6-L water bath (Model-DH003BH, Daeho Co, Namyangu-si, South Korea) maintained at 43°C. This procedure was aimed at stabilizing the baseline finger temperature and

Table. Summary of the subjects' physical characteristics^a

Subject	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m ²)	Body fat (%)
n = 10	24 ± 2	175.0 ± 5.1	71.3 ± 7.4	23.3 ± 2.6	16 ± 6

BMI, body mass index.

^a Values are mean ± SD.

preventing possible vasoconstriction of the finger vasculature before cold water immersion. The stabilized finger was immediately dried by a towel after the warm water immersion, and the subjects then underwent each experimental condition before cold water immersion for CIVD observation.

The 6 experimental conditions were characterized by either a control (NCAFF) or caffeine (CAFF) trial followed with rest on a chair, submaximal exercise, or maximal exercise. In CAFF, the subjects chewed the 3 pieces of caffeine gum during the 10-minute rest period, whereas they remained seated for rest in NCAFF after the warm water immersion. For the exercise intervention, the subjects performed a graded treadmill exercise (Bruce protocol) to the point of 70% or 100% maximal oxygen consumption ($\dot{V}O_{2\max}$), based on the results of aerobic fitness testing during the initial health screening. We chose these 2 exercise intensities to discern physical activities that may require submaximal and maximal efforts outdoors. The exercise duration for 70% and 100% $\dot{V}O_{2\max}$ trials differed among subjects as their maximal aerobic capacity was different. To ensure that the target exercise intensity was reached, oxygen consumption was also monitored using a portable metabolic monitoring system (K4b², COSMED, Rome, Italy). On completion of the exercise, subjects rested on a chair for 5 minutes before performing the CIVD protocol, whereas in nonexercise trials, they continued resting on a chair for an additional 15 minutes to roughly match these exercise–rest duration (Figure 1).

For the CIVD protocol, the subjects immersed the middle finger to the level of the proximal interphalangeal joint in a 6-L water bath maintained at 5°C for 20 minutes while quietly seated on a chair and placing their hand on a secured rail maintained at heart level. These water temperature and measurement procedures have

been suggested as less painful and effective in obtaining CIVD results.^{4,22}

MEASUREMENT AND INSTRUMENTATION

Finger temperature (T_f) was continuously measured with a copper-constant thermocouple (Model-T type, Barnant Co, Barrington, IL) attached to the nail bed of the middle finger of the dominant hand using surgical tape (Model-Transpore, 3M, St. Paul, MN). We chose to measure T_f from the fingernail bed rather than nail pad or fingertip as it has been suggested that the day-to-day reproducibility of CIVD in the immersed finger is better in the nail bed²³ because of a rich supply of arteriovenous anastomoses (AVA). Core temperature (T_{re}) was measured using a rectal probe (Model-J type 600/1000, Barnant Co) inserted 10 cm beyond the anal sphincter. All temperature data were monitored and stored through a customized data acquisition system incorporated with a data logger (Model-2635A, Fluke, Cleveland, OH).

Previous studies of CIVD^{23–25} used different aspects of CIVD parameters, but commonly included the components of time, temperature, amplitude, and number of occurrences of CIVD, yet no standardized measurement criteria exist. Thus, we chose to analyze the following 5 parameters of the first CIVD cycle in the current investigation, as depicted in Figure 2: (1) minimum finger temperature ($T_{f\cdot\min}$), (2) maximum finger temperature ($T_{f\cdot\max}$), (3) difference between $T_{f\cdot\min}$ and $T_{f\cdot\max}$ ($T_{f\cdot\text{diff}}$), (4), time from immersion to $T_{f\cdot\min}$, also called onset time (Δt_{onset}), and (5) time from $T_{f\cdot\min}$ to $T_{f\cdot\max}$, known as peak time (Δt_{peak}).

Caffeine was administered as 3 pieces of chewing gum (Model-Stay Alert, Amurrol Confections, Yorkville, IL), which contain 100 mg of caffeine per piece (total 300 mg). Relative bioavailability of this caffeine formulation

Figure 1. Summary of experimental procedure and time line. CIVD, cold-induced vasodilation; $\dot{V}O_{2\max}$, maximum oxygen consumption.

Figure 2. Temperature and time parameters of cold-induced vasodilation responses. $T_{f,\min}$, minimum finger temperature; $T_{f,\max}$, maximum finger temperature; $T_{f,\text{diff}}$, difference between $T_{f,\min}$ and $T_{f,\max}$; Δt_{onset} , time from immersion to $T_{f,\min}$; and Δt_{peak} , time from $T_{f,\min}$ to $T_{f,\max}$.

was reported as 87% per 100 mg to the systemic circulation.²⁶ Although previous studies^{8,9,18} investigating ergogenic effects of caffeine on exercise used variable doses, depending on the exercise performance of interest (eg, strength vs endurance), typical doses used for an ergogenic purpose range between 2 and 6 mg/kg body weight as comparable to our experimental dose (approximately 4.2 mg/kg body weight).

For the norepinephrine assay, 10 mL blood samples were drawn from a midantecubital vein using a micro-syringe and stored in a blood collection tube containing an anticoagulant agent (K2 EDTA). The samples were immediately centrifuged at 3000g for 10 minutes, and separated plasma aliquots were stored in a freezer (-35°C) for later assay. Norepinephrine concentrations in plasma were determined using high-performance liquid chromatography (HPLC) with electrochemical detection (Acclaim, Bio-Rad, Hercules, CA). The HPLC method, which involves a physical separation of the compound mixture in liquid for analytical quantification, has been widely validated for the analysis of plasma catecholamines and is known to be advantageous in sensitivity for the detection of small changes in trace concentrations.²⁷

STATISTICS

The CIVD parameters were first calculated individually and presented as mean and standard deviation for each experimental group. Two-way analysis of variance was performed to determine the effect of caffeine and exercise on CIVD parameters, followed by multiple comparisons with Scheffé correction. For a significant F ratio, paired Student's t test and one-way analysis of variance were performed for caffeine and exercise effects on the CIVD parameters, respectively. Statistical significance was set at

a probability value less than .05, and all analyses were performed using a statistical software package (SPSS v.12.0, IBM, Somers, NY).

Results

A graded exercise test during a health screening showed their average maximal oxygen consumption to be $56.4 \pm 2.8 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, indicating a high aerobic fitness level (upper 95th percentile) for their age group.^{16,28} All subjects completed the 6 experimental trials, and there was no statistical difference in baseline measurements with a smaller day-to-day variability, shown as T_{re} , $36.86^{\circ}\text{C} \pm 0.06^{\circ}\text{C}$; HR, 65 ± 6 beats/min; and USG, 1.024 ± 0.004 (normal hydration status in USG units). Exercise duration for subjects to complete their 70% and 100% $\dot{V}\text{O}_{2\text{max}}$ trials was 8.9 ± 0.9 minutes and 12.4 ± 0.8 minutes, respectively (Table).

There was no main effect of caffeine ($P > .05$; $F = 1.050$) on $T_{f,\min}$, but exercise was significantly ($P < .001$; $F = 39.646$) associated with higher $T_{f,\min}$ in both NCAFF (mean $\pm$ SD [95% CI]: $9.08 \pm 1.27^{\circ}\text{C}$ [8.17–9.99 $^{\circ}\text{C}$]; $13.02 \pm 2.13^{\circ}\text{C}$ [11.49–14.55 $^{\circ}\text{C}$]; and $13.25 \pm 1.63^{\circ}\text{C}$ [12.09–14.43 $^{\circ}\text{C}$] in rest, submaximal, and maximal exercise, respectively) and CAFF trials ($8.76 \pm 1.39^{\circ}\text{C}$ [7.77–9.77 $^{\circ}\text{C}$]; $12.50 \pm 1.91^{\circ}\text{C}$ [11.13–13.88 $^{\circ}\text{C}$]; and $12.79 \pm 1.20^{\circ}\text{C}$ [11.93–13.66 $^{\circ}\text{C}$]; Figure 3A). Both caffeine ($P = .001$; $F = 13.244$) and exercise ($P = .019$; $F = 4.253$) affected $T_{f,\max}$ significantly (NCAFF, $15.98 \pm 1.04^{\circ}\text{C}$ [15.23–16.73 $^{\circ}\text{C}$]; $16.18 \pm 1.56^{\circ}\text{C}$ [15.07–17.30 $^{\circ}\text{C}$]; and $15.14 \pm 1.52^{\circ}\text{C}$ [14.05–16.23 $^{\circ}\text{C}$] in rest, submaximal, and maximal exercise, respectively, and CAFF, $13.56 \pm 1.19^{\circ}\text{C}$ [12.72–14.51 $^{\circ}\text{C}$]; $15.52 \pm 1.31^{\circ}\text{C}$ [14.59–16.46 $^{\circ}\text{C}$]; and $14.39 \pm 1.43^{\circ}\text{C}$ [13.37–15.42 $^{\circ}\text{C}$]) in the way in which caffeine hinders the rise of

Figure 3. Summary of temperature parameters in cold-induced vasodilation under rest and submaximal (submax) and maximal (max) exercise conditions for trials with (CAFF) and without (NCAFF) caffeine. (A) Minimum finger temperature, (B) maximum finger temperature, and (C) difference between minimum and maximum finger temperature. * significantly different at $P < .05$; ** significantly different at $P < .01$; ≠ significantly different from Rest condition at $P < .05$. Values are mean and SD ($n = 10$).

$T_{f, \max}$, as this effect is somewhat blunted by exercise (Figure 3B). Consequently, $T_{f, \text{diff}}$ was also significantly affected by both caffeine ($P = .011$; $F = 6.881$) and exercise ($P < .001$; $F = 56.341$; NCAFF, $6.89 \pm 1.56^\circ\text{C}$ [5.78 – 8.01°C]; $3.16 \pm 1.22^\circ\text{C}$ [2.29 – 4.05°C]; and $1.88 \pm 0.53^\circ\text{C}$ [1.05 – 2.27°C] in rest, submaximal, and maximal exercise, respectively, and CAFF, $4.79 \pm 1.23^\circ\text{C}$ [3.91 – 5.68°C]; $3.02 \pm 1.77^\circ\text{C}$ [1.75 – 4.29°C]; and $1.59 \pm 0.62^\circ\text{C}$ [1.15 – 2.04°C]). $T_{f, \text{diff}}$ between

NCAFF and CAFF was most prominent in the rest condition (Figure 3C).

There was no main effect of caffeine on Δt_{onset} ($P > .05$; $F = 2.358$), although Δt_{onset} was continuously shorter in NCAFF (169.0 ± 83.2 seconds [109.5 – 228.5 seconds]; 107.6 ± 83.4 seconds [47.9 – 167.2 seconds]; and 77.8 ± 45.8 seconds [45.0 – 110.6 seconds] in rest, submaximal, and maximal exercise, respectively) than CAFF (189.6 ± 78.2 seconds [133.7 – 245.5

seconds]; 155.3 ± 65.8 seconds [108.2–202.4 seconds]; and 90.8 ± 40.2 seconds [62.1–119.5 seconds]). However, exercise significantly shortened Δt_{onset} ($P < .001$; $F = 9.661$) in NCAFF and CAFF trials (Figure 4A). Similarly, Δt_{peak} did not significantly differ between NCAFF (268.4 ± 122.9 seconds [180.4–356.4 seconds]; 133.3 ± 80.0 seconds [76.0–190.6 seconds]; and 89.8 ± 40.6 seconds [60.7–118.9 seconds] in rest, submaximal, and maximal exercise, respectively) and CAFF (226.6 ± 90.5 seconds [161.9–291.3 seconds]; 126.3 ± 86.2

seconds [64.6–187.9 seconds]; and 77.7 ± 43.0 seconds [46.9–108.5 seconds]; $P > .05$; $F = 0.912$), with significantly shorter Δt_{peak} in exercise trials ($P < .001$; $F = 21.048$; Figure 4B).

Plasma norepinephrine concentration was significantly less in NCAFF (105.6 ± 29.5 pg/mL [84.5–126.8 pg/mL]; 199.6 ± 89.6 pg/mL [135.5–263.6 pg/mL]; and 361.5 ± 171.3 pg/mL [238.9–484.0 pg/mL] in rest, submaximal, and maximal exercise, respectively) than CAFF (290.6 ± 113.0 pg/mL [209.8–371.4 pg/mL];

Figure 4. Summary of time parameters in cold-induced vasodilation and plasma norepinephrine concentration under rest and submaximal (submax) and maximal (max) exercise conditions for trials with (CAFF) and without (NCAFF) caffeine. (A) Onset time, (B) peak time, and (C) plasma norepinephrine concentration. * significantly different at $P < .05$; ** significantly different at $P < .001$; $\neq$ significantly different from Rest condition at $P < .05$. Values are mean and SD ($n = 10$).

278.1 $\pm$ 91.4 pg/mL [212.7–343.5 pg/mL]; and 399.8 $\pm$ 125.5 pg/mL [310.0–489.5 pg/mL]; $P = .001$; $F = 12.130$) and also significantly increased from rest to exercise ($P < .001$; $F = 14.677$; Figure 4C).

Discussion

The purpose of the present study was to investigate the effects of prior caffeine intake on CIVD responses to peripheral cold exposure, and thus provide perspectives on whether ingesting caffeine (eg, coffee) before engaging in outdoor activities in the cold could potentially influence the body's protective mechanism against cold stress. The study findings demonstrate that caffeine intake negatively affects CIVD responses by attenuating a rise of finger temperature without any thermogenic effect present on $T_{f, \min}$, which resulted in a lower mean finger temperature during cold water immersion in the rest condition, but not after exercise interventions. However, there was no significant effect of caffeine on the time parameters of the CIVD cycle, whereas exercise interventions significantly shortened Δt_{onset} and Δt_{peak} compared with rest.

Caffeine has been thought to promote thermogenesis and increase short-term metabolism, total daily energy expenditure, and body temperature.^{10,17} However, these added thermogenic effects were not observed in studies that involved exercise^{11–13,29} or cold exposure.^{14,15} It has also been reported that the thermal state of the body significantly influences CIVD, such that hyperthermia increases $T_{f, \min}$ and $T_{f, \max}$ and hypothermia decreases these finger temperature parameters.^{21,24,25,30} Thus, it is not unreasonable to speculate that our finding of $T_{f, \min}$ maintained at a similar level between NCAFF and CAFF (Figure 3A) indirectly indicates the absence of caffeine-induced thermogenesis in this study. Interestingly, $T_{f, \max}$ was also significantly lower in CAFF than NCAFF (Figure 3B), although baseline T_{re} and T_f were homogeneously stabilized before all experimental trials. This is likely because of caffeine-induced reduction in blood flow to the periphery. Caffeine is a well-known antagonistic agent to adenosine receptors,^{18,31} a mode of action that in some tissues (eg, skeletal muscle) includes circulatory vasodilation.³² Therefore, caffeine-induced blockade of adenosine receptors significantly attenuates forearm blood flow and increases vascular conductance,^{11,29} which we speculate as a main cause of the significantly decreased $T_{f, \max}$ in the CAFF trials.

Another factor that could have contributed to a lower $T_{f, \max}$ and altered time components of CIVD responses concomitantly in CAFF (Figures 4A and 4B) may be elevated norepinephrine. Although caffeine's impact on the sympathetic nervous system¹⁸ or norepinephrine con-

centration is equivocal,^{14,17} in our results post-trial norepinephrine concentrations were consistently higher in CAFF than NCAFF (Figure 4C). On exposure to cold, cutaneous vasoconstriction occurs rapidly via sympathetic activation of norepinephrine that stimulates α -adrenergic receptor activity.^{1,2} Elevation of norepinephrine is prominent during rest and exercise in cold air,¹⁴ and cold stimuli on a greater body surface area (eg, hand vs finger immersion) evokes stronger sympathetic stimulation, and thus a higher concentration of norepinephrine.³³ Previous studies observed an absence of CIVD in the rat tail³⁴ and significantly attenuated CIVD responses in human fingers³⁵ owing to elevated vasoconstriction when norepinephrine was experimentally infused, thereby suggesting that interference of adrenergic neurotransmission under severe vasoconstriction occurred as a result of excessive norepinephrine and may have an influence on CIVD emergence.⁴

Nonetheless, this caffeine-induced reduction in blood flow seems to be attenuated or somewhat masked by exercise, as indicated by elevated $T_{f, \min}$ and smaller $T_{f, \text{diff}}$, as well as accelerated Δt_{onset} , in exercise compared with rest conditions in the present study. This probably resulted from postexercise vasodilation in the periphery caused by a partial or combined effect of reduction in forearm vascular resistance³⁶ or elevated body temperature, promoting more blood to the finger for heat dissipation. The latter explanation seems to be more probable given the ample evidence in previous studies.^{24,25,30,32} Unfortunately, we were not able to identify a level of body temperature elevation and its relative contribution to forearm blood flow in association with CIVD responses between rest and exercise conditions because of the absence of blood flow measurements and discontinuation of T_{re} recordings after experimental stabilization, which may be identified as a current study limitation.

In addition to the measurement limitation discussed above, some study limitations could be identified in the present study design. First, we did not perform pharmacokinetic analysis for the actual caffeine absorption rate in the body during CAFF trials. However, a previous study²⁶ examining the same caffeine gum reported that approximately 85% of the caffeine dose is released in the first 5 minutes of administration and consequent caffeine concentration in plasma reaches the maximum level in approximately 40 to 80 minutes.²⁴ Thus, it is possible that the caffeine concentration in our subjects did not reach its maximum concentration at the beginning of the cold water immersion, but may likely have reached at least a near-maximum level while performing the CIVD protocol. Second, application of the present data to the general population or habitual caffeine users is limited,

although caffeine impact on CIVD responses was clear among our young, healthy, and nonhabitual caffeine subjects in the present study. Lastly, we studied male subjects only, but purposely excluded female subjects as their vascular reactivity to cold exposure was known to be different from male subjects.⁴ Thus, the data presented herein need to be interpreted with caution.

In conclusion, the present study is the first to investigate the effects of caffeine intake on CIVD responses of the cold water immersed finger. The study results demonstrated that caffeine intake before peripheral cold exposure (finger immersion) does not enhance but rather significantly attenuates CIVD temperature responses together with an alteration in time responses. Meanwhile, these responses appear to be somewhat offset after exercise, in which postexercise vasodilation for heat dissipation of elevated body temperature during exercise occurs. The present findings, therefore, suggest that caffeine intake may adversely affect the protective mechanisms of the body responding to peripheral cold exposure, as opposed to current concepts of caffeine ergogenicity. In practical terms, the present results also imply, given the study limitations, that a common practice of drinking hot beverages containing caffeine before cold exposure may not be an advantageous strategy in terms of protecting local cold injuries.

Acknowledgments

The authors express sincere gratitude to the subjects for their enthusiastic participation in the study.

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