Ingestion of carbonated water increases middle cerebral artery blood velocity and improves mood states in resting humans exposed to ambient heat stress

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\textbf{ABSTRACT}

Sugar-free carbonated water is consumed worldwide. The consumption of carbonated water is high in summer, when the heat loss responses of sweating and skin vasodilation are activated, and thermal perceptions (thermal sensation and comfort) and mood states are negatively modulated. However, whether ingesting carbonated water under ambient heat exposure modulates cerebral blood flow index, heat loss responses, thermal perceptions, and mood states remains to be determined. In this study, 17 healthy, habitually active, young adults (eight women) ingested 4°C noncarbonated or carbonated water under 37°C ambient heat-stressed resting conditions. Both drinks increased the middle cerebral artery mean blood velocity, an index of cerebral blood flow, and mean arterial pressure, with carbonated water exhibiting higher elevations than noncarbonated water ($P < 0.05$). However, the heart rate, sweat rate, and skin blood flow during and after drinking remained unchanged between the two conditions ($P > 0.05$). The thermal sensation and comfort after drinking remained unchanged between the two conditions ($P > 0.05$); but, a drink-induced reduction in sleepiness was higher, and drink-induced elevations in motivation and exhilaration were higher after ingesting carbonated water than after ingesting noncarbonated water ($P < 0.05$). The analyses suggest that in humans under ambient heat-stressed resting conditions, ingestion of cold carbonated water increases the cerebral blood flow index, blood pressure, motivation, and exhilaration, whereas it decreases sleepiness relative to ingestion of noncarbonated cold water. However, ingestion of cold carbonated water fails to modulate thermoregulatory responses and thermal perception as opposed to noncarbonated cold water.

\section*{New and noteworthy}

Sugar-free carbonated water is consumed worldwide, with higher consumption in summer than in other seasons. In this study, we found that ingestion of carbonated water increased the cerebral blood flow index, blood pressure, motivation, and exhilaration, whereas it decreased sleepiness relative to ingestion of noncarbonated water without influencing heat loss responses and thermal perceptions. These responses might ensure positive behavioral changes, such as improved work productivity under heat stress conditions.

\section*{1. Introduction}

The sugar-free carbonated water market is increasingly expanding \cite{1}. This could be due to individuals’ preference for sugar-free carbonated water over sugary carbonated drinks, as the latter may lead to a positive energy balance, and increase chances of type 2 diabetes and cardiovascular disease \cite{2,3}. The higher ambient temperatures lead to greater consumption of drinks, including carbonated drinks \cite{4}, and thus, drink consumption is higher in summer than that in other seasons \cite{5}. As the ambient temperature may continue to increase due to global warming, the sales of carbonated water may also rise continuously. However, whether and how ingestion of carbonated water modulates...
the body’s function, perception, and mood under ambient heat-stressed conditions remain to be determined.

Early studies reported that ingestion of non-carbonated water caused a prolonged pressor response in older adults or in patients with autonomic failure [6,7]. By contrast, this response was not clearly observed in healthy young adults in early studies [7,8], possibly due to augmented arterial baroreflex control of muscle sympathetic nerve activity [9]. However, subsequent studies reported that the pressor response can occur in young adults [10,11], though the response is relatively transient [11–13]. A recent work by Kubota et al. [11] reported that cold carbonated water ingestion resulted in a greater transient increase in mean arterial pressure relative to non-carbonated cold water ingestion under thermoneutral condition (28 °C). This may reflect increased sympathetic nerve activity evoked by tingling sensation associated with activation of nociceptors in the oral cavity via conversion of CO₂ to carbonic acid, a response that is mediated by carbonic anhydrase [14]. The pressor response associated with ingestion of carbonated water may increase the cerebral blood flow via elevations in blood pressure and perfusion pressure [15]. However, increased sympathetic nerve activity associated with ingestion of carbonated water may lead to cerebral vasconstriction, as the cerebral vessels constrict in response to elevated cerebral sympathetic nerve activity [16]. Thus, direct assessment is required to delineate if ingestion of carbonated water increases the cerebral blood flow in ambient heat-stressed resting humans. Cerebral blood flow plays a key role in regulating oxygen supply and heat removal in the brain, as well as intracranial pressure. Therefore, it is physiologically important to assess how carbonated water ingestion modulates cerebral blood flow.

Heat stress is known to activate the heat loss responses of sweating and cutaneous vasodilation [17]. Although drinking water does not modulate the heat loss responses under euhydration conditions [18], whether drinking carbonated water modulates thermal sweating and cutaneous vasodilation remains unclear. Studies reported that augmented sympathetic nerve activity elicited by handgrip exercise or postexercise arm occlusion stimulated sweating [14,19–22], with little or relatively small changes in cutaneous vascular tone [19,20,22–24] under ambient heat exposure or heat stress mediated by water perfusion suit. Hence carbonated water ingestion, which appears to increase sympathetic nerve activity as mentioned above, might increase sweating, though this needs to be directly examined.

Heat stress negatively modulates thermal perceptions (i.e., person feels uncomfortable) and mood states [25,26]. Carbonated water ingestion can also modulate several mood states and perceptions [27]. For example, ingestion of carbonated water increases fullness [28] whereas it reduces neural processing of sweetness [29] and thirsty sensation [30]. Since increasing CO₂ concentration in beverage can increase cold sensation of beverage [31], carbonated water ingestion might positively modulate thermal perceptions such as thermal sensation (i.e., person feels less hot) and thermal comfort during heat stress. Indeed, thermal sensation during heat stress is reduced by augmented cooling sensation at mouth by -menthol mouthwash [32].

Therefore, in this study, we evaluated the hypothesis that ingestion of carbonated water increases blood pressure, cerebral blood flow index, and sweating, and positively modifies thermal perceptions (i.e., person feels less hot and more comfortable) and mood (i.e., person feels more motivated, exhilarated, and less sleepy) in resting humans exposed to ambient heat. The present study would provide insights into if carbonated water ingestion can be used as an intervention that mitigates hypotension, cerebral hypoperfusion, syncope, hyperthermia, and/or negative perceptive and mood responses occurring during heat stress.  

2. Materials and methods

2.1. Ethics approval

The study was approved by the Human Subjects Committee of the University of Tsukuba (no. 020–133), and conducted in agreement with the Declaration of Helsinki (revised in 2013), except for registration in a database. Written informed consent was obtained from all participants prior to their participation in the study.

2.2. Participants

Seventeen healthy, habitually active young adults (eight women) were enrolled in the study. A power analysis was performed based on previous data, wherein the effect of carbonated water on the heart rate was assessed [28]. We believe that this is the only relevant study that can be used for a power analysis. We found that a minimum of 15 participants would be required to detect any changes in heart rate associated with the ingestion of carbonated water, with at least 80% statistical power (α=0.05). The participants’ age, body mass, height, and body mass index, presented as mean ± standard deviation, were 25±5 years, 65.2 ± 15.2 kg, 1.68±0.08 m, and 23.0 ± 4.1 kg m⁻², respectively. All participants were non-smokers, and none reported any medical conditions or the administration of prescription medications. None of the women were taking oral contraceptives. All women were assessed during the self-reported early follicular phase (≤6 days after the start of menstruation), wherein both estrogen and progesterone levels are low, such that the potential influence of sex hormones on responses to ingestion of water can be minimized.

2.3. Experimental procedures

Participants were asked to abstain from consuming caffeinated drinks and alcohol 12 h before the experiment. The participants were also advised to avoid intense exercise at night. Ingestion of supplements and over-the-counter drugs was not allowed ≤48 h before the day of experiment. The purpose of the study was not revealed to the participants, nor was the involvement of a soft drink company mentioned, in order to avoid any preconceived bias. On the day of the experiment, the participants fasted for ≥2 h before and throughout the experiment. To ensure euhydration, they were asked to drink 200 mL of water (Oishii Mizu, Asahi Soft Drink Co., Ltd, Tokyo, Japan) approximately 2 h before the experiment. On arrival, all participants voided their bladders, and the urine samples were obtained to assess urine specific gravity, a hydration marker. Furthermore, we measured weight of the participants (model ICS429; Mettler Toledo, Schwerzenbach, Switzerland), and they were instructed to self-insert a rectal probe (401, NikkisoTherm Co., Ltd, Tokyo, Japan). The participants entered a room (Fuji Medical Science Co., Ltd, Chiba, Japan) controlled to 37 °C ambient temperature and 50% relative humidity. The participants quietly rested on the seat of a customized semi-recumbent bicycle (Model B18E, Monark, Stockholm, Sweden) for 60 min while all equipments were attached. The baseline measurements were obtained for 10 min. Next, participants were asked to ingest either noncarbonated water (Oishii Mizu) or carbonated water (Wilkinson, Asahi Soft Drink Co., Ltd, Tokyo, Japan) using a straw within approximately 30 s. The volume of each drink was 150 mL for men and 100 mL for women. These volumes were determined based on results of a pilot study by our group to avoid excess stress associated with ingestion of carbonated water (e.g., elevated urinary intention). The temperature of the drinks was maintained at cold temperature of 4 °C, as carbonated water is often consumed at cold temperatures. Also, cooler temperature of drink possibly increases the effect of CO₂ on perceptions including coldness [31]. While drinking, one examiner held a cup containing either noncarbonated or carbonated water near the participant’s mouth to avoid their contact with water cup. After drinking, the participants rested for at least 15 min, allowing the assessment of prolonged cardiovascular responses after drinking [10,11], if any. Participants ingested both the drinks twice. The order of the four drinking procedures was randomized and counterbalanced as much as possible.
2.4. Measurements

2.4.1. Cardiovascular responses

The heart rate was measured every 5 s using a heart rate monitor (RS400 Poral, Kempele, Finland) in eight participants. The heart rate and root mean square of successive R-R interval differences, the latter being an index of the parasympathetic nerve activity, were assessed using a different heart rate monitor (V800, Poral, Kempele, Finland) in nine participants. During the clamp method, the arterial blood pressure was measured beat-to-beat using finger photoplethysmography system (Finometer, Finapres Medical System, Amsterdam, Netherlands) from the right middle finger that was placed at the heart level. The mean arterial pressure was estimated as the diastolic arterial pressure plus one-third of the pulse pressure. The stroke volume was estimated using the model flow method [33]. The cardiac output was calculated as the stroke volume multiplied by the heart rate. The total peripheral resistance was calculated as the mean arterial pressure divided by cardiac output. The beat-to-beat middle cerebral artery blood velocity was measured using transcranial Doppler ultrasound system (EZ-Dop, Compumedics Germany GmbH, Singen, Germany). A 2-MHz probe was placed in the left cranial temporal bone window. The sample volume depth was set at 43–62 mm. The sampling volume width was set at 8 mm. Analog data were digitized using AD converter (Power Lab; AD Instruments, Australia) at a sampling frequency of 200 Hz. The middle cerebral artery blood velocity signal was not successfully obtained in two participants (one man and one woman), and thus, we could analyze data for 15 participants. To account for the changes in perfusion pressure on the cerebral blood flow, the middle cerebral artery vascular conductance index was evaluated as the middle cerebral artery mean blood velocity divided by mean arterial pressure. The cutaneous blood flow index was assessed at the forearm and chest using a laser-Doppler flowmeter (ALF21, Advance, Tokyo, Japan), with values presented in mV. The cutaneous vascular conductance was calculated as the laser-Doppler signal divided by mean arterial pressure to account for the changes in perfusion pressure due to technical difficulties, the middle cerebral artery blood velocity, blood pressure, heart rate, total peripheral resistance, and chest and forearm cutaneous vascular conductance in two participants, and chest and forearm skin blood flow in one participant could not be measured successfully.

2.4.2. Respiratory responses

The respiratory variables (minute ventilation, oxygen uptake, CO₂ elimination, and end-tidal CO₂ partial pressure) were measured breath-by-breath using electric gas flowmeter (AE300s, Minato Medical Science, Osaka, Japan). A hot-wire-type mass flow sensor was used to estimate the respiratory volumes. The gas sampling rates for O₂ and CO₂ partial pressures were 0.15 L/min. Calibration was performed on the electric gas flowmeter immediately before the start of the measurement, using a syringe with a known volume of 2 L and reference gasses at known concentrations. To obtain inspiratory and expiratory gasses, a mouthpiece was inserted in the participant’s mouth with their nose closed using a nose clip throughout the experiment, except when drinking. The mouthpiece and nose clip were reattached 1 min after the completion of each drinking. Thus, we were unable to obtain respiratory data during the first 1 min post-drinking period.

2.4.3. Body temperatures

The rectal temperature was monitored with thermocouple (401, NikkisoTherm Co., Ltd) that was inserted approximately 15 cm from the external anal sphincter. The skin temperature was monitored using thermocouples attached to seven skin sites on the left side: the forehead, chest, forearm, hand, thigh, calf, and foot. All temperature variables were recorded every 1 s and stored in a data logger (WE7000, Yokogawa, Tokyo, Japan). Mean skin temperature was calculated based on the equation proposed by Harnd & Dubois [34]. Due to technical difficulties, the rectal and skin temperatures were not successfully collected in one participant.

2.4.4. Sweating responses

The sweat rates at the chest and forearm were assessed using the sweat capsule method. A sweat capsule with 2.83 cm² area was attached to the chest and forearm. Dry compressed N₂ gas equilibrated to 37 °C was supplied from gas tanks to each capsule at a rate of 1.5 L/min regulated by a mass flow controller (DF-200, Kofloc, Kyoto, Japan). A capacitance hygrometer (HMT330, Vaisala, Helsinki, Finland) was used to measure the relative humidity and temperature in the effluent air from the sweat capsule every 1 s and data was stored in a data logger (WE7000, Yokogawa). Long vinyl tubes were used to ensure connections between the N₂ gas tank and sweat capsule (inlet), and between the sweat capsule and capacitance hygrometer (outlet). The N₂ flow rate, area under the capsule, and measured relative humidity and temperature were used to calculate the local sweat rate presented in mg·min⁻¹·cm⁻², as explained in our previous study [35]. Due to technical difficulties, the chest and forearm sweat rate in one participant could not be successfully measured.

2.5. Perceptions and mood states

Using a visual analog scale on a 100 mm horizontal straight line, corresponding to a score from 0 to 100, we assessed four subjective perceptions: thermal sensation (0 = cold, 100 = hot), thermal comfort (0 = uncomfortable, 100 = comfortable), stimulating feelings of the mouth (0 = none, 100 = very stimulating), and abdominal fullness (0 = none, 100 = very full). Additionally, we assessed four mood states: exhilaration for the mouth and whole body, assessed separately (0 = none, 100 = very exhilarating); sleepiness (0 = none, 100 = very sleepy); and motivation (0 = none, 100 = very motivated). All perceptions and mood states were assessed at baseline (immediately before drinking), and 1, 6 and 12 min after drinking. On all occasions, the participants marked all the variables within approximately 30 s. The stimulating feeling of the mouth in one participant could not be successfully measured due to a misunderstanding of the meaning, leading to n = 16 for data analysis.

2.6. Urine specific gravity

The urine specific gravity was measured using refractometer (T38XRI, Atago Co., Ltd., Tokyo, Japan).

2.7. Data analysis

Physiological variables were averaged over the last 5 min of each baseline period, at 1-min drinking period, and at 1 min intervals during post-drinking period (i.e., 0–1 min, 5–6 min, and 11–12 min, except for 5–6 min and 11–12 min for respiratory variables). Physiological, perceptual, and mood state data measured twice during each drink trial were averaged and used for data presentation and statistical analyses. Responses were similar between the first and second measurements. The changes (Δ) in physiological variables (except respiratory variables) during ingestion of drink from the baseline were calculated for each trial. Changes (Δ) in perceptual and mood state variables and stimulating feeling for the mouth from the baseline to 1-min post-drinking period were calculated for each drink trial. The difference in Δ values between the noncarbonated and carbonated water drinks was calculated to obtain the carbonated water-mediated changes and was used for correlation analyses. Investigators were not blinded to outcomes during data collection and analyses.

2.8. Statistics

Data were analyzed using Prism 8 software (GraphPad, CA, USA). The normal distribution of variables was verified using a Q-Q plot. We
employed a two-way repeated measures analysis of variance for variables with repeated factors of time and drink type. The Greenhouse-Geisser correction was employed when violating the assumption of sphericity. When the main effect or interaction was significant, post hoc analysis was performed for pairwise comparisons, with P-values adjusted by the Bonferroni procedure. The Pearson’s correlation coefficient was used to relate the two variables. As both the mean arterial pressure and cardiac output can modulate the cerebral blood flow [15, 36, 37], we performed correlation analyses to assess relation between the cerebral artery mean blood velocity and mean arterial pressure and cardiac output. Correlation analyses were also performed between all perceptive and mood state variables and the middle cerebral artery mean blood velocity, as the cerebral blood flow may modulate behavioral changes [38]. Furthermore, for exploratory purpose, correlation analyses between all variables and stimulation feeling of the mouth, the latter being a major sensation associated with ingestion of carbonated water, were assessed. All data are reported as mean ± 95% confidence interval, unless otherwise noted. A P < 0.05 was considered to be statistically significant.

3. Results

The urine specific gravity measured before the experiment was 1.014 ±0.004, indicating euhydration (<1.025 of urine specific gravity [39]).

3.1. Cardiovascular responses

Drinking water transiently increased the middle cerebral artery mean blood velocity (P < 0.05), and this response was greater with carbonated water than with noncarbonated water (Fig. 1A-C). A similar response was also observed for the mean arterial pressure (Fig. 1D-F). The heart rate increased in response to the ingestion of either noncarbonated or carbonated water (P < 0.05), but it was not different between the two drinks (Fig. 1G-I). A similar response was also observed for the cardiac output and root mean square of successive R-R interval differences (SI Appendix, Fig. S1A-F). A drink-induced change in the total peripheral resistance differed between the two drinks, such that the total peripheral resistance while drinking was elevated in the carbonated than that in noncarbonated water condition (Fig. 1L). The middle cerebral artery vascular conductance index remained unchanged between the two drink trials throughout the study (data not shown).

3.2. Thermoregulatory responses

The sweat rate and skin blood flow during and after drinking remained unchanged between ingestion of the noncarbonated and carbonated drinks regardless of the skin sites (chest and forearm) (Fig. 2A-L). Furthermore, the cutaneous vascular conductance measured at the chest and forearm remained unchanged between the two drinking conditions (data not shown). Additionally, the core and skin temperatures remained unchanged during and after drinking, with no differences between the two trials (SI Appendix, Fig. S1G-L).

3.3. Respiratory variables

Minute ventilation, oxygen uptake, and CO₂ output were not different between the two drink trials at any time point (all P > 0.127 for a main effect of drink and an interaction between time and drink; data not shown). The end-tidal CO₂ partial pressure at baseline remained unchanged between trials (P = 0.946). The end-tidal CO₂ partial pressure recorded post-ingestion was not presented because several artifacts associated with ingestion of carbonated water were detected on the end-tidal CO₂ partial pressure.

3.4. Perceptions and mood states

We found that drinking water transiently reduced thermal sensation (feeling of less hot) and thermal comfort (feeling of more comfort) (P < 0.05) without differences between the two drink conditions (Fig. 3A-D). Drinking transiently increased exhilaration of the participants (both for mouth and whole body) (P < 0.05), and this response was greater in the carbonated drink than in noncarbonated drink conditions (Fig. 3E-H). Sleepiness was reduced following drinking (P < 0.05), and the response was augmented more by ingestion of carbonated water than by noncarbonated water (Fig. 3I and J). Motivation was increased by drinking either noncarbonated or carbonated water (P < 0.05), with carbonated water exhibiting greater elevation than noncarbonated water (Fig. 3L). Stimulating feelings for the mouth were elevated after the ingestion of carbonated water (Fig. 3M and N). Abdominal fullness increased after drinking (P < 0.05), and this response tended to be greater in carbonated relative to noncarbonated water trials (Fig. 3O and P).

3.5. Correlative analyses

The mean arterial pressure, and not cardiac output, correlated with the middle cerebral artery mean blood velocity (Fig. 4A and B). Further, motivation positively correlated, and thermal comfort negatively correlated with the middle cerebral artery mean blood velocity (Fig. 4C and D). Stimulating feeling for the mouth positively correlated with exhilaration of the mouth and whole body (Fig. 4E and F).

4. Discussion

The heart rate and mean arterial pressure were both transiently elevated during the drinking of noncarbonated water. The swallowing reflex [40,41] that can increase the heart rate and blood pressure may be involved in the tachycardia and pressor responses observed in the present study. Additionally, a beverage temperature of 4 °C may be another factor mediating the pressor response, as a lower drink temperature increases blood pressure [11,42]. It is noteworthy that the mean arterial pressure was more elevated in the carbonated than that in noncarbonated water trials in the present study, which is consistent with a recent work by Kubota et al. [11] who showed that a drink induced transient increase in mean arterial pressure was greater in 4 °C carbonated water relative to non-carbonated 4 °C water conditions.

Activation of TRPV1 in the swallowing-related regions (e.g., larynx) can augment the swallowing reflex [43]. The carbonated water-induced stimulation of TRPV1 [44] may augment the swallowing reflex observed in the present study, that led to a greater elevation in the mean arterial pressure. As the heart rate and estimated cardiac output were not different between the two drink trials, the augmented pressor response could be primarily due to increased peripheral vasoconstriction. Consistent with this, a drink-induced increase in the total peripheral resistance was higher in the carbonated than that in noncarbonated water trials. This response, in part, may be mediated by increases in vasopression that can cause vasoconstriction and thus pressor response. Indeed, TRPV1, which is activated by carbonated water (as noted above), may increase vasopression release [45]. The increased peripheral vasoconstriction associated with ingestion of carbonated water may not be explained by the skin microvascular response, as the skin blood flow and skin vascular conductance remained unaffected between the two drink trials after ingestion of carbonated water. As elevations in the core and skin temperatures attenuate skin vasoconstriction during leg dependency [46], any vasoconstriction effect associated with the ingestion of carbonated water may be abolished by elevated skin temperatures mediated by exposure to ambient heat. It is possible that the splanchnic and/or skeletal muscle vasoconstriction was elicited during ingestion of carbonated water owing to the increased sympathetic nerve activity, explaining the higher total peripheral resistance.

Further, we found that the cerebral blood flow index, as assessed by
Fig. 1. Cardiovascular responses to ingestion of noncarbonated and carbonated water. The middle cerebral artery mean blood velocity, mean arterial pressure, heart rate, and total peripheral resistance data are presented. (A, D, G, J) Every 10-s data, (B, E, H, K) averaged data over each stage, and (C, F, I, L) drink-induced changes from baseline are presented for all four variables. Two-way repeated measure ANOVA is performed on averaged data presented in B, E, H, and K. * vs. noncarbonated water ($P < 0.05$) assessed by Bonferroni procedure. Data are presented as mean ± 95% confidence intervals for A, B, D, E, G, H, J, and K, or mean with individual data for C, F, I, and L ($N = 15$).
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Fig. 2. Thermoregulatory responses to ingestion of noncarbonated and carbonated water. The sweat rate and skin blood flow, both measured at the chest and forearm, are presented. (A, D, G, J) Every 10-s data, (B, E, H, K) averaged data over each stage, and (C, F, I, L) drink-induced changes from baseline are presented for all four variables. Two-way repeated measure ANOVA is performed on averaged data presented in B, E, H, and K. * vs. noncarbonated water (P < 0.05) assessed by Bonferroni procedure. Data are presented as mean ± 95% confidence intervals for A, B, D, E, G, H, J, and K, or mean with individual data for C, F, I, and L (N = 16).
Fig. 3. Perceptive and mood state responses to ingestion of noncarbonated and carbonated water. Thermal sensation and comfort, exhilaration of the mouth and whole-body, sleepiness, motivation, stimulating feeling of the mouth, and abdominal fullness are presented. (A, C, E, G, I, K, M, O) Averaged data over each stage, and (B, D, F, H, J, L, N, P) drink-induced changes from baseline are presented for all variables. Two-way repeated measure ANOVA is performed on averaged data presented in A, C, E, G, I, K, M, and O. * vs. noncarbonated water ($P < 0.05$) assessed by Bonferroni procedure. Data are presented as mean ± 95% confidence intervals for A, C, E, G, I, K, M, and O, or mean with individual data for B, D, F, H, J, L, N, and P ($N = 17$ except $n = 16$ for stimulating feeling of the mouth).
the middle cerebral artery mean blood velocity, increased in response to ingestion of carbonated and noncarbonated water, with the magnitude being greater in the carbonated water condition than that in noncarbonated water condition. Therefore, although the sympathetic nerve activity may be increased by ingestion of carbonated water, sympathetic nerves regulating the cerebral arteries [16] may not be sufficiently activated to mediate robust cerebral vasoconstriction. As minute ventilation and CO$_2$ output at the baseline and after ingestion were similar between the noncarbonated and carbonated water conditions, CO$_2$ elimination through breathing and CO$_2$ production in the body may be largely unaffected by the ingestion of carbonated water. In this case, the arterial CO$_2$ pressure that plays a major role in the regulation of cerebral blood flow [47–49] would not be modulated by the ingestion of carbonated water. Furthermore, cardiac output, a factor that possibly modulates the cerebral blood flow [36,37], failed to differ between the trials during ingestion and was not significantly correlated with the middle cerebral artery mean velocity. A recent study suggests that the cerebral blood flow can alter in response to changes in the arterial pressure [15]. Thus, the elevated mean arterial pressure elicited by ingestion of carbonated water may elevate the middle cerebral artery mean blood velocity. This finding is further supported by the positive correlation between the mean arterial pressure and middle cerebral
artery mean blood velocity. Additionally, the correlation remained significant despite removing an outlier that exhibited marked reductions in the middle cerebral artery mean blood velocity and mean arterial pressure.

Ingestion of carbonated water failed to alter sweating and cutaneous blood flow responses relative to ingestion of noncarbonated water. This may indicate that sympathetic nerve activation associated with carbonated water ingestion does not modulate the heat loss responses of sweating and cutaneous vasodilatation. This is in contrast to previous studies showing that augmentation of sweating under heat stressed conditions elicited by handgrip exercise or postexercise arm occlusion [14,19-22], each can mediate sympathetic activation. It may be that the magnitude of activation of sympathetic nerves elicited by carbonated water ingestion is smaller than that elicited by handgrip exercise or postexercise arm occlusion. Alternatively, since pressor response evoked by carbonated water ingestion was relatively transient, more prolonged sympathetic nerve activation is required to modulate sweating response. No effect of carbonated water ingestion on the sweating and cutaneous blood flow responses indicates that heat dissipation may be largely unaffected by ingestion of carbonated water. Along this line, the body core and skin temperatures remained unchanged during and after drinking in the present study. Furthermore, thermal sensation and comfort were reduced by drinking water irrespective of the drink type (feeling of less hot and more thermal comfort) that may be, at least partly, due to cold (4 °C) drinks, but these variables remained unchanged between the two drink conditions. Interestingly, there was a negative correlation between the middle cerebral artery mean blood velocity and thermal comfort that warrants future studies to elucidate the mechanisms underlying this relationship.

It is noteworthy that ingestion of carbonated water increased exhilaration and motivation, whereas it decreased sleepiness more than that with ingestion of noncarbonated water. Thus, the results of the present study suggest that ingestion of carbonated water can positively modulate mood. The positive correlation between the middle cerebral artery mean blood velocity and motivation may indicate that increased cerebral perfusion associated with carbonated water ingestion is a key factor that increases motivation. It is known that acute changes in the cerebral blood flow fail to modulate cognitive functions [50], but changes in the cerebral blood flow associated with marijuana smoking lead to behavioral changes [38]. If the cerebral metabolism remained unchanged by ingestion of carbonated water, increases in the cerebral blood flow can reduce CO2 levels in the cerebral tissues [51] and brain temperature [52]. Moreover, increases in the cerebral blood flow may increase shear stress that further activates endothelial cells that release several substances, such as nitric oxide [53]. These alterations associated with ingestion of carbonated water may modulate motivation. In contrast, stimulating the feeling of the mouth by ingestion of carbonated water positively correlated with exhilaration. This implies that altering the mouth sensation is a factor that can change mood.

4.1. Limitations

There are several limitations to note. First, during drinking we were not able to measure end-tidal CO2 pressure, an index of partial pressure of arterial CO2 that can modulate cerebral blood flow [47]. Thus, we do not know the extent to which partial pressure of arterial CO2 modulated our results, though the between-trial difference in end-tidal CO2 pressure appears to be small as discussed above. Second, we do not know if temperature of drink modulated responses observed. We elected to use cold drink as this is what typically consumed in a real life especially in summer. However, given that lower temperature in the stomach attenuates heat loss responses [54], carbonated water induced activation of sweating, if present, might be attenuated by cold temperature of drink used. Third, we do not know if the response observed during drinking was in part due to interaction with investigators (e.g., investigator asked participants to drink beverages and mark on visual analogue scales). It should be highlighted that the timing of interactions with investigators was well matched between the two drink conditions. Thus, any difference between the two trials should reflect the effect of adding CO2 to cold water. Fourth, we tested responses in hot environment only as we were interested in responses under heat stress. Hence, we cannot delineate if different ambient temperature modulates carbonated water-induced responses. Fifth, our visual analog scale did not have extreme values for thermal sensation (e.g., extremely hot) and comfort (e.g., extremely uncomfortable). Our results might have been different if the scale had extreme values.

4.2. Practical applications

The consumption of sugar-free carbonated water is high in the summer [5]. The results of the present study suggested that ingestion of carbonated water fails to modulate the heat loss responses of sweating and cutaneous vasodilation, core and skin temperatures, or thermal perceptions. Thus, ingestion of carbonated water under heat-stressed conditions may not influence the heat balance and behavior temperature regulation, and thus, the risk of heat-related injuries. In contrast, ingestion of carbonated water mediates pressor response and a concomitant elevation in cerebral blood flow index. Therefore, carbonated water ingestion might be used to counteract hypotension, cerebral hypoperfusion, and syncope that possibly occurring under heat stressed conditions. Moreover, ingestion of carbonated water improved several mood states, such as exhilaration, sleepiness, and motivation, the latter being possibly due to increased cerebral blood flow. Thus, the heat-related reduction in work productivity [55] may be partly countered by ingesting carbonated water at workplaces. However, it should be noted that responses observed by ingestion of carbonated water were relatively transient. To benefit the effects of carbonated water ingestion for longer period, carbonated water might need to be ingested over longer period, which requires future direct assessment.

5. Conclusions

The study suggests that under ambient heat-stressed resting conditions, ingestion of carbonated water increases the blood pressure, cerebral blood flow index and improves mood states, whereas it decreases sleepiness. However, ingestion of carbonated water fails to modulate thermoregulatory responses or thermal perception (Fig. 5).

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CRediT authorship contribution statement

Naoto Fujii: Conceptualization, Methodology, Data curation, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition. Yufuko Kataoka: Investigation, Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. Yin-Feng Lai: Investigation, Data curation, Formal analysis, Writing – review & editing. Nanae Shirai: Investigation, Writing – review & editing. Hideki Hashimoto: Investigation, Writing – review & editing, Funding acquisition. Takeshi Nishiyasu: Resources, Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare no competing interest. Asahi Soft Drinks Co., Ltd. had no control over the interpretation, writing, or publication of this work. The results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. H.H. is an employee of Asahi Soft Drinks Co. Ltd.
Data availability

Data will be made available on request.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1016/j.physbeh.2022.113942.

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