ORIGINAL ARTICLE

Cardiovascular responses to water ingestion at rest and during isometric handgrip exercise

Goncalo V. Mendonca · Micael S. Teixeira ·
Fernando D. Pereira

Abstract Water drinking activates sympathetic vasoconstriction in healthy young adults; however, this is not accompanied by a concomitant increase in resting blood pressure. It is not known whether the water pressor effect is unmasked by a physiological condition such as exercise. Therefore, we examined the effect of water ingestion (50 vs. 500 mL) on the cardiovascular and autonomic responses to isometric handgrip in 17 healthy participants (9 men, 8 women, aged 28.4 ± 9.7 years). Beat-to-beat blood pressure and R–R intervals were recorded in both conditions at rest (pre- and post-ingestion) and during handgrip at 30% of maximal voluntary contraction. R–R series were spectrally decomposed using an autoregressive approach. Water ingestion did not interact with the increase in mean arterial pressure (MAP) from rest to exercise, which was similar between conditions. In contrast, there was an overall bradycardic effect of water and this was accompanied by increased high frequency power (condition main effect, $p < 0.05$). When the differences in high frequency power between conditions were controlled for, MAP was significantly higher after drinking 500 mL of water (condition main effect, $p < 0.05$). In addition, water ingestion attenuated the increase in the low to high frequency power ratio from rest to handgrip (interaction effect, $p < 0.05$). In conclusion, the rise in blood pressure post-water ingestion is prevented both at rest and during isometric handgrip. Interestingly, this is not sustained after controlling for the enhanced vagal drive caused by water ingestion. Therefore, the mechanisms underlying this response most likely depend on reflex bradycardia of vagal origin.

Keywords Blood pressure · Autonomic function · Water · Exercise

Introduction

Acute water ingestion has several effects on human cardiovascular autonomic regulation and has been successful in minimizing negative orthostatic symptoms by increasing blood pressure and total peripheral resistance (Jordan et al. 2000; Lu et al. 2003; Schroeder et al. 2002; Scott et al. 2001). Ingestion of ~500 mL of water augments sympathetic vasoconstrictor tone, as shown by increases in muscle sympathetic nerve activity, calf vascular resistance, and plasma norepinephrine (Jordan et al. 2000; Schroeder et al. 2002; Scott et al. 2001). However, while in patients with abnormal autonomic control and in the elderly water ingestion has been shown to elicit an acute rise in blood pressure between 11 and 30 mmHg (Jordan et al. 1999, 2000), this has not been seen in younger healthy individuals (Routledge et al. 2002; Scott et al. 2001). Thus, previous research indicates that an enhanced sympathetic drive is a normal response to water drinking but paradoxically an associated pressor effect is only present in those with autonomic dysfunction. There is compelling evidence that this may be due to a concomitant increase in cardiovagal drive, which prevents a rise in the blood pressure of healthy persons by means of reflex bradycardia (Brown et al. 2005; Routledge et al. 2002).

Although most of these studies suggest the existence of compensatory mechanisms that buffer the increase in blood

G. V. Mendonca (✉) · M. S. Teixeira · F. D. Pereira
Center of Human Performance (CIPER),
Faculty of Human Kinetics, Technical University of Lisbon,
Estrada da Costa, Cruz Quebrada, 1495-688
Cruz Quebrada Dafundo, Lisbon, Portugal
e-mail: gvmendonca@gmail.com

pressure after water ingestion in healthy persons, it is not known whether this is sustained during acute autonomic provocative tasks (i.e., isometric handgrip exercise). Isometric handgrip exercise is a simple, non-invasive and well validated test of autonomic function that elicits both positive chronotropism and inotropism (Khurana and Stetty 1996; Seals et al. 1994). According to past research, increased heart rate and blood pressure during handgrip are mediated by a combination of vagal withdrawal and sympathetic activation (Iellamo et al. 1999; Kjaer and Secher 1992; Seals et al. 1994; Ebert 1986). Therefore, given that isometric handgrip is accompanied by substantial vagal withdrawal, it is possible that the physiological ability to counteract the water pressor effect might be limited under such form of exercise. According to this hypothesis, the bradycardic effect of water ingestion would likely be reduced during isometric handgrip; thus limiting the primary mechanism by which the cardiovascular system compensates for the increased peripheral alpha adrenergic stimulation involved in the water pressor effect (McHugh et al. 2010). Ultimately, the systemic effects of water ingestion might be manifested during isometric handgrip and lead to an unfavorable hemodynamic profile during exercise. Support for this hypothesis has been generated by data showing that the bradycardic effect of facial cooling is attenuated during exercise; thus unmasking the pressor effect of facial cooling, not otherwise seen at rest (Smith et al. 1997). Because the reflex adjustments in cardiovascular function secondary to water ingestion are quite similar to those seen after facial cooling (i.e. cardiovagal activation, bradycardia, and peripheral vasoconstriction), it is possible that the water pressor response may well be unmasked during sustained isometric handgrip performed by healthy adults (Brown et al. 2003). Yet, the acute effects of water ingestion on the cardiovascular and autonomic responses to isometric exercise have not been previously studied.

Our main purpose was to determine, in a comprehensive study, whether pre-exercise water ingestion affects the cardiovascular and autonomic responses to isometric handgrip exercise in healthy adults. Therefore, we compared the changes in beat-to-beat blood pressure and cardiac autonomic function, in transition from rest to isometric handgrip, after the ingestion of 50 and 500 mL of water.

Methods

Subjects

We studied 17 healthy participants on no medications (9 men and 8 women, age: 28.4 ± 9.7 years, height: 170.8 ± 6.0 cm, body mass: 67.4 ± 9.3 kg and body mass

index: 23.0 ± 2.3 kg/m^2) with normal blood pressure (systolic and diastolic values repeatedly <140/90 mmHg). Participants were all non-obese and free from any known cardiovascular or metabolic diseases, as assessed by medical history. Previous studies have reported fluctuations in autonomic function during the menstrual cycle (Sato et al. 1995; Saeki et al. 1997). For this reason, all women were studied in the early follicular phase of their menstrual cycle. Each participant was requested to avoid heavy exercise for at least 24 h before testing and to have nothing to eat or drink in the morning prior to testing. Participants were also asked to empty their bladders just before testing. Written informed consent was obtained from each participant and procedures were thoroughly explained before data collection. This study was carried out with the approval from the University's Institutional Review Board and in accordance with the Declaration of Helsinki.

Study design

Participants were evaluated over the course of two visits on separate days at approximately the same time of the day (between 0700 and 1100 hours). The participants acted as their own controls and they all performed resting and static handgrip protocols under the following two conditions within a 1-week period: (1) 25-min post-ingestion of 50 mL of water and; (2) 25-min post-ingestion of 500 mL of water. The order of testing was randomized. During the first visit, standing height and body mass measurements were taken with the participants wearing light-weight clothes and no shoes. Height was obtained using a stadiometer with measures obtained to the nearest 0.5 cm. Body mass was measured on a balance-beam scale. Body mass index (BMI) was calculated by dividing the participants' mass in kilograms by the square of their height in meters. Subsequently, participants were asked to assume the seated position and maximal grip strength was measured using the dominant hand with an electronic handgrip dynamometer (TSD121C, Biopac Systems, Santa-Barbara Calif.) interfaced with a computer with visual feedback on the computer monitor. Participants were given standardized encouragement to produce maximal effort. Maximal voluntary contraction (MVC) was determined using the highest of three maximal contractions. After several minutes of seated rest to ensure complete hemodynamic recovery, testing was started with a 3-min resting period (baseline). Subsequently, in a randomized fashion, participants ingested either 50 (control) or 500 mL (experimental) of water at room temperature within 90 s and remained quietly seated for another 25 min. The period of 25 min was chosen because previous studies have shown that the physiological responses to water ingestion are maximal at about 20- to 30-min post-ingestion (Routledge et al. 2002;

Brown et al. 2005; Jordan et al. 2000; Scott et al. 2001). Testing was then resumed for another 3 min of rest, followed by a 3-min isometric handgrip contraction at 30% of MVC. We chose a 3-min contraction period to standardize the length of contraction, and a pilot testing revealed that 3 min was the longest contraction period possible to ensure inclusion of both men and women. During the contraction phase of the test, participants received visual feedback on the computer monitor to help them produce the correct force required. Testing was carried out in a laboratory with an environmental temperature of between 21 and 24°C and a relative humidity of between 44 and 56%.

Hemodynamic and autonomic measurements

Non-invasive continuous blood pressure recordings were obtained from the middle finger of the non-dominant hand using a Finometer device (TNO Biomedical Instrumentation, Amsterdam, The Netherlands). The blood pressure signals were sampled and stored in a computer for posterior analysis. R–R intervals were obtained by means of a Polar R–R recorder (Polar R–R recorder RS 800 G3, Polar Electro, Kempele, Finland) at a frequency of 1,000 Hz, providing an accuracy of 1 ms for each R–R interval. Blood pressure and R–R interval signal processing was performed on 3-min epochs corresponding to different physiological conditions.

The R–R signal was inspected and edited for ectopic beats and artifacts using linear interpolation. Power spectral analysis was performed based on autoregressive modeling, following data detrending and re-sampling (4 Hz) (Kubios HRV Analysis Software 2.0 for Windows, University of Kuopio, Finland). The frequency domain variables included the high (HF: 0.15–0.4 Hz) and the low frequency (LF: 0.04–0.15 Hz) bands. It is widely accepted that the HF power reflects vagal modulation of heart rate and that both the LF power and the ratio of LF/HF reflect a complex interplay between sympathetic and parasympathetic modulation. The physiological meaning of the very low frequency power assessed from short-term recordings is less defined and its interpretation is not recommended when analysing power spectra density results (Camm et al. 1996). Finally, the ratio of LF/HF was also calculated and used as an index of sympathovagal balance (Pagani et al. 1986). All data acquisition and post-acquisition analyses were carried out in accordance with standards put forth by the Task Force of the European Society of Cardiology and North American Society of Pacing and Electrophysiology (Camm et al. 1996).

Statistical analysis

All data are reported as mean ± SD, unless otherwise specified. Before comparing both conditions, data were tested for normality and homoscedasticity with the Kolmogorov–Smirnov and Levene's tests, respectively. Intraindividual differences between cardiovascular and spectral heart rate variability (HRV) variables at baseline (pre-ingestion) were compared by paired t tests. A two-way ANOVA [condition (50 mL of water vs. 500 mL of water) by time (rest vs. handgrip at 30% MVC)] with repeated measures was conducted on all dependent variables to compare differences in mean arterial pressure (MAP) and HRV between post-ingestion of 50 (control) and 500 mL (experimental) volumes. When a significant interaction was observed, post hoc one-way ANOVAs were used to determine where the difference occurred. Low and high frequency power were transformed to their natural logarithm for statistical analysis because of their skewed distribution.

Previous studies have suggested that increased cardiovagal modulation after water ingestion prevents the rise in the blood pressure of healthy adults (Brown et al. 2005; Routledge et al. 2002). In agreement with past research, we also obtained an overall increase in HF power both at rest and during handgrip post-500 mL of water. These differences in HF power between conditions (delta HF power: 50 vs. 500 mL) at each time point (rest vs. handgrip) were highly correlated with each other, and therefore, they were reduced to a single component using factor analysis. Subsequently, we repeated the statistical analysis on MAP using this single delta HF component as a covariate (ANCOVA). This was done with the purpose of exploring whether the increased cardiovagal modulation, resulting from the ingestion of 500 mL of water, might eventually compensate for the effects of heightened sympathetic vasomotor discharge on blood pressure. Finally, we also examined the Pearson correlation coefficients between delta heart rate and delta HF power, from 50 to 500 mL, at rest and during handgrip. All statistical calculations were computed using SPSS version 17.0 and a significance level of $p < 0.05$ was used.

Results

All the cardiovascular and spectral HRV variables were similar between testing days before water ingestion (baseline) (Table 1). Figure 1 shows that, despite MAP increased in transition from rest to handgrip at post-ingestion conditions (time main effect: $F = 139.7$, $p < 0.05$), there were no differences between 50- and 500-mL volume at either time point. In contrast, as shown in Fig. 2a, there was an overall decrease in heart rate after drinking 500 mL of water compared to that seen in the 50-mL condition (condition main effect: $F = 8.1$, $p < 0.05$). Nevertheless, heart rate increased similarly between conditions from rest to

Table 1 Cardiovascular variables and spectral heart rate variability at rest before the ingestion of 50 and 500 mL of water

Variables	50-mL trial	500-mL trial
Systolic arterial pressure (mmHg)	111.6 ± 10.5	111.8 ± 7.7
Diastolic arterial pressure (mmHg)	69.8 ± 8.2	69.9 ± 8.3
Mean arterial pressure (mmHg)	86.8 ± 8.7	86.9 ± 7.7
Heart rate (bpm)	67.6 ± 11.8	66.8 ± 12.4
HF (ln ms^2)	6.4 ± 1.3	6.5 ± 1.3
LF (ln ms^2)	6.7 ± 1.1	6.9 ± 0.9
LF/HF	2.5 ± 3.1	2.1 ± 1.5

Values are mean ± SD. HF and LF are the natural logarithm (ln)

HF raw high frequency power, *LF* raw low frequency power, *LF/HF* low to high frequency power ratio
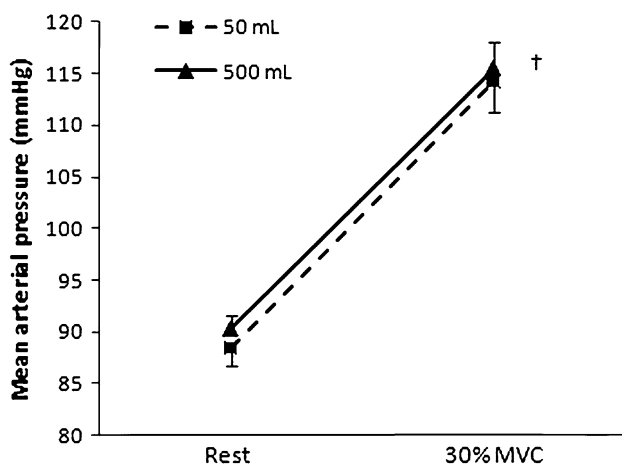

Fig. 1 Mean arterial pressure in transition from rest to isometric handgrip at 30% of maximal voluntary contraction after ingestion of 50 and 500 mL of water. Values are mean ± SEM. [†]Time main effect, $p < 0.05$

static handgrip (time main effect: $F = 91.1$, $p < 0.05$). As for heart rate, but in the opposite direction, the ingestion of 500 mL of water resulted in an overall increase in HF power compared to the ingestion of 50 mL (condition main effect: $F = 6.5$, $p < 0.05$). After water ingestion, HF power also decreased significantly from rest to handgrip conditions and this was similar between 50- and 500-mL volume (time main effect: $F = 43.0$, $p < 0.05$) (Fig. 2b). In addition, Fig. 2c shows that the LF power was not affected by drinking 500 mL of water at rest or during handgrip. Moreover, despite significant (time main effect: $F = 26.1$, $p < 0.05$), the change in LF power from rest to handgrip was similar between conditions. There was a significant interaction for the LF/HF ratio (interaction effect: $F = 5.9$, $p < 0.05$), thus indicating that the overall change in this parameter differed between conditions. Specifically, while the LF/HF ratio was significantly increased from rest to handgrip in the 50-mL condition ($p < 0.05$); this did not occur after drinking 500 mL of water (Fig. 2d).

We also intended to explore whether enhanced cardiovagal modulation after 500 mL of water, both at rest and during exercise, partially prevented the increase in MAP at post-ingestion conditions. Because there was an overall increase in resting and exercise HF power after drinking 500 mL of water compared to that occurring post-50 mL, we reduced these differences between conditions to one single component (delta HF component) which was then used for the covariance adjustment. The results from the ANCOVA, controlling for the delta HF component from 50 to 500 mL of water, are depicted in Fig. 3. In contrast to that seen in Fig. 1, when the differences in HF power between conditions (500 vs. 50 mL) were controlled for, the overall MAP was significantly higher after drinking 500 mL of water (condition main effect: $F = 5.0$, $p < 0.05$). Finally, the decrease in heart rate from 50 to 500 mL of water was significantly correlated with the changes obtained in raw HF power both at rest ($r = -0.77$, $p < 0.05$) and during static handgrip ($r = -0.85$, $p < 0.05$).

Discussion

The main finding of our study is that, in healthy adults, pre-exercise ingestion of 500 mL of water did not increase the pressor effect induced by sustained isometric handgrip at 30% MVC. Our data also indicate that the rise in blood pressure after 500 mL of water was prevented by a concomitant bradycardic effect. Importantly, this occurred in both resting and exercise conditions. Moreover, such reduction in heart rate was accompanied by heightened HF power spectral modulation which strongly suggests that it was of vagal origin. The significant correlations obtained between the increase in HF power and the bradycardic effect after 500 mL of water further support an increased cardiovagal drive post-water ingestion. We also found that the increased cardiovagal drive, resulting from drinking 500 mL of water, most likely contributed for attenuating the pressor effect of water ingestion, both at rest and during exercise. In support of this contention, our results of similar blood pressure between conditions (50 vs. 500 mL) were not sustained after covarying MAP response with the enhancements in HF power that were secondary to 500 mL of water. Specifically, after controlling for the effects of water ingestion on HF power, 500 mL of water led to an overall higher blood pressure compared to that seen after 50 mL. Therefore, we provide preliminary evidence that increased cardiovagal drive post-water ingestion corresponds to a compensatory mechanism that effectively counteracts the water pressor effect at rest and during exercise.
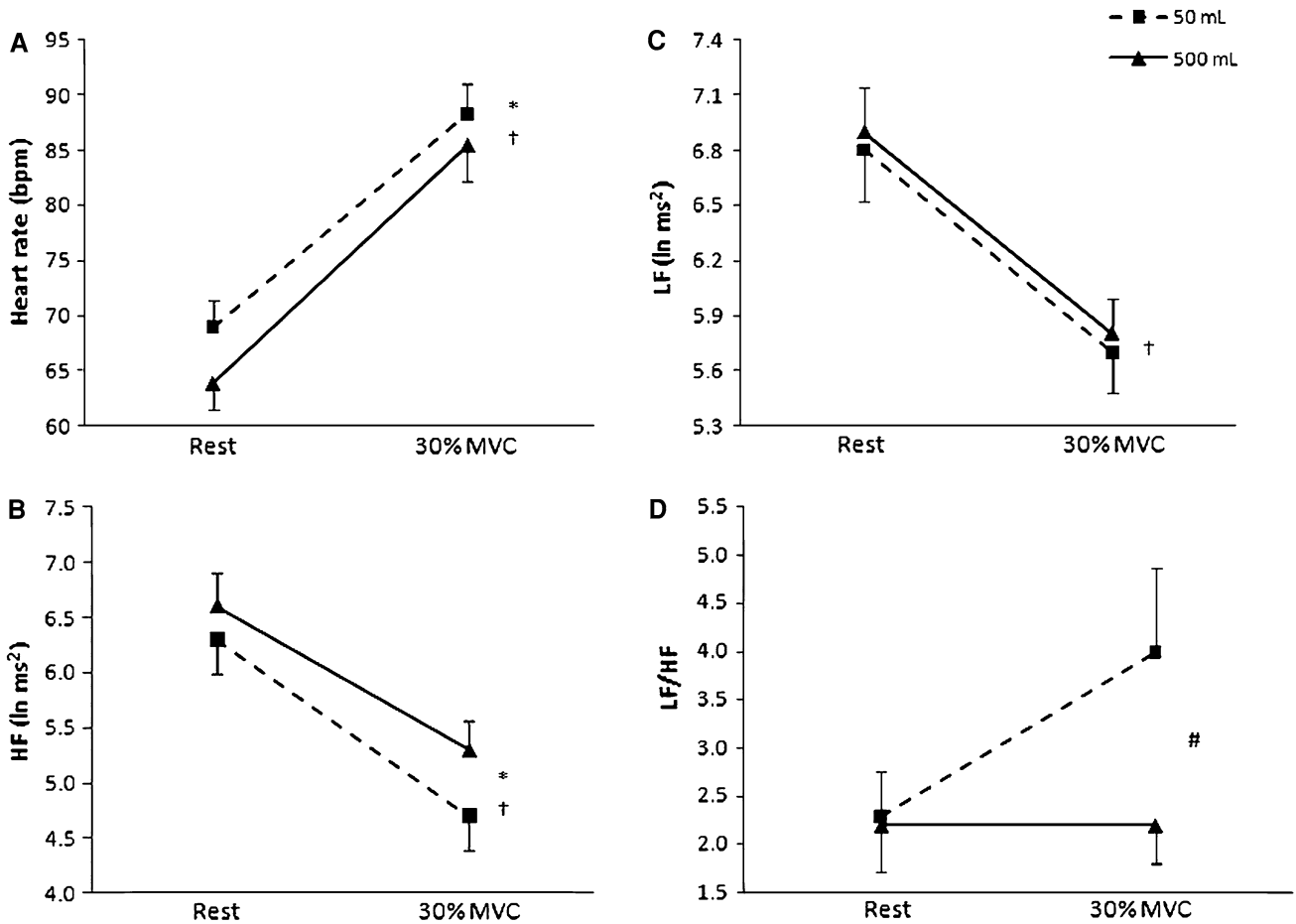
Fig. 2 Heart rate and spectral components of heart rate variability in transition from rest to isometric handgrip at 30% of maximal voluntary contraction after ingestion of 50 and 500 mL of water. **a** Heart rate; **b** high frequency power (HF); **c** low frequency power (LF); **d** low to high frequency power ratio (LF/HF). HF and LF are the natural logarithm (ln). Values are mean ± SEM. [†]Time main effect, *condition main effect, [#]interaction effect, $p < 0.05$
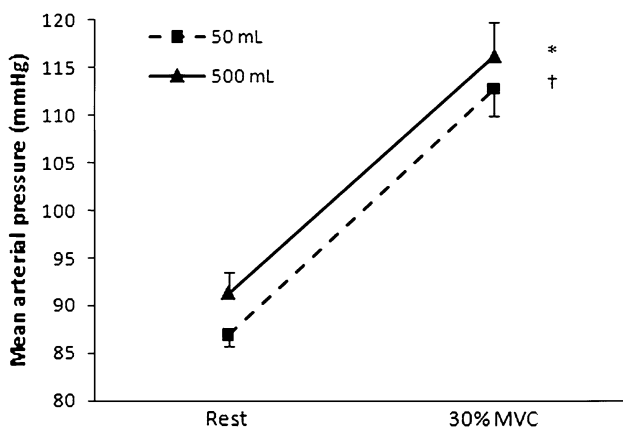

Fig. 3 Mean arterial pressure in transition from rest to isometric handgrip at 30% of maximal voluntary contraction after ingestion of 500 and 50 mL of water, adjusted for delta HF power component (reduced component of delta HF power at rest and during exercise between conditions). Values are mean ± SEM. [†]Time main effect, *condition main effect, $p < 0.05$

Water ingestion has a large pressor effect in autonomic failure. This effect is also present in older healthy individuals, is antagonized by ganglionic blockade with trimethaphan, and is associated with increases in plasma norepinephrine and in muscle sympathetic activity (Jordan et al. 2000; Scott et al. 2001). According to previous research, the pressor response to water ingestion is independent of changes in plasma renin activity, vasopressin or blood volume (Jordan et al. 2000) and there is compelling evidence that it is secondary to the activation of the transient receptor potential cation channel family (*TRPV* osmolarity-sensitive Ca^{2+} channels) within the hepatic portal circulation (McHugh et al. 2010). Persons with preserved autonomic function do not manifest an increased blood pressure after water drinking, and this has been shown to associate with ensuing bradycardia which is paired by increased cardiovagal modulation (Routledge et al. 2002; Brown et al. 2005). We hypothesized that this

effect of water might be dissipated during sustained isometric handgrip; a physiological condition which results in considerable vagal withdrawal (Kjaer and Secher 1992).

Drinking 500 mL of water did not interact with the hemodynamic response to handgrip compared to that seen after the ingestion of 50 mL. Therefore, contrary to that hypothesized, water ingestion did not elicit increased blood pressure during isometric exercise in healthy adults and this is similar to that reported at rest (Brown et al. 2005; Routledge et al. 2002; Jordan et al. 2000; Scott et al. 2001; Shannon et al. 2002). Moreover, our findings indicate that the underlying mechanism preventing the increase in blood pressure after 500 mL of water ingestion was similar between resting and exercise conditions. Specifically, at 25-min post-ingestion there was an overall decrease in heart rate, both at rest and during handgrip, which most likely compensated the increased sympathetic vasoconstrictor discharge induced by 500 mL of water (Scott et al. 2001) by means of decreased cardiac output. Interestingly, we provide evidence that such compensatory bradycardia was of vagal origin. This is supported by the significant correlations obtained between the increase in HF power, a widely accepted marker of vagal modulation of heart rate, and bradycardia, both at rest and during handgrip, after ingestion of 500 mL of water (Camm et al. 1996). Therefore, by showing that decreased heart rate and heightened vagal modulation after water ingestion also occurred during isometric exercise, our results corroborate and further extend those of previous studies. In fact, given that vagal modulation is associated with a cardioprotective effect (Billman 2002), water ingestion may play an important role in enhancing myocardial electrical stability during autonomic provocative tasks. This assumes even greater relevance in the context of exercise; a physiological condition characterized by an increased risk of cardiovascular events (Albert et al. 2000).

To the best of our knowledge, the exact mechanism by which drinking 500 mL of water stimulates vagal modulation remains largely unknown. Brown et al. (2005) have shown a concomitant increase in HF power modulation and baroreflex sensitivity after a similar volume of ingested water. Despite the non-redundancy between both indices (Ferrari et al. 1995), this suggests that increased vagal modulation may be dependent on baroreflex-mediated compensation for increased sympathetic vasomotor discharge. From a functional perspective, it is plausible that the water-dependent enhancements in cardiovagal drive may partially attenuate, by means of secondary bardycardia, the effects of increased sympathetic vasomotor discharge on blood pressure. In support of this hypothesis, we found that adjusting MAP response for the gains in HF power after 500 mL of water resulted in significant differences between conditions (50 vs. 500 mL). Interestingly, the overall MAP

was higher after drinking 500 mL compared to 50 mL and this was only seen after including the covariate in the model (Fig. 3). This corroborates the notion that an increased vagal modulation of the sinus node actively blunts the rise in the blood pressure of healthy persons after water ingestion by means of a bradycardic effect. Importantly, it also agrees with data from previous studies showing that, in patients whose hearts had been vagally denervated by cardiac transplantation, there is an exacerbated pressor response to water drinking (Routledge et al. 2002).

According to our findings, the ingestion of 500 mL of water did not influence the LF spectral power at rest or during isometric handgrip. In consonance with past research, LF power decreased during static exercise and this occurred similarly between conditions (50 vs. 500 mL) (Iellamo et al. 1999; Stewart et al. 2007). In contrast, even though the resting LF/HF ratio was similar between conditions; drinking 500 mL of water prevented its increase from rest to exercise and this was different from that seen in the 50 mL condition. As previously shown, the LF/HF ratio typically increases during sustained isometric handgrip (Stewart et al. 2007). This is caused by a gradual enhancement in sympathetic activation which, combined with vagal withdrawal, accounts for the changes in heart rate after the first minute of handgrip (Stewart et al. 2007; Iellamo et al. 1999; Kjaer and Secher 1992; Seals et al. 1988; Stratton et al. 1983). Taken together, our findings suggest that pre-exercise water ingestion (500 mL) prevented the increase in the LF/HF ratio from rest to isometric handgrip. Therefore, under these conditions, the positive chronotropic response from rest to handgrip may have been primarily dependent on vagal withdrawal. However, since the magnitude of change in heart rate from rest to exercise was similar between conditions, it is difficult to provide a definite explanation for the discrepancies in the LF/HF ratio behavior and its role in regulating the chronotropic response to handgrip. Nevertheless, as noted by Goldberger et al. (2001), the relationship between heart rate and HF spectral power is largely non-linear. Thus, we speculate that the changes seen in resting HF power after 500 mL water ingestion may have relocated this relationship towards a steeper portion of the curve. As a consequence, this may have possibly attenuated the physiological increase in the LF/HF ratio, which would otherwise be associated with the chronotropic response to handgrip.

In conclusion, we found that pre-exercise water drinking does not implicate a greater magnitude of blood pressure increase in transition from rest to sustained isometric handgrip in healthy adults. We also provide preliminary evidence that the mechanisms preventing the rise in blood pressure after water ingestion involve a bradycardic effect of vagal origin, both at rest and during exercise conditions.

Finally, water ingestion attenuated the shift in the cardiac sympathovagal balance towards sympathetic dominance in response to isometric handgrip. Thus, it is likely that the chronotropic response to handgrip after water ingestion relies primarily on vagal withdrawal. Furthermore, because water ingestion is known to increase plasma norepinephrine and peroneal sympathetic nerve activity (Lu et al. 2003; Scott et al. 2001), this also supports the contention that sympathetic suppression may be specifically targeted to the heart.

References

Albert C, Mittleman M, Chae C, Lee I, Hennekens C, Manson J (2000) Triggering of sudden death from cardiac causes by vigorous exertion. N Eng J Med 343:1355–1361

Billman G (2002) Aerobic exercise conditioning: a nonpharmacological antiarrhythmic intervention. J Appl Physiol 292:446–454

Brown C, Sanya EO, Hilz MJ (2003) Effect of cold face stimulation on cerebral blood flow in humans. Brain Res Bull 61:81–86

Brown C, Barberini L, Dulloo A, Montani J (2005) Cardiovascular responses to water drinking: does osmolality play a role? Am J Physiol Integr Comp Physiol 289:R1687–R1692

Camm A, Malik M, Bigger J, Günter B, Cerutti S, Choen R et al (1996) Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate variability: standards of measurement, physiological interpretation and clinical use. Circulation 93:1043–1065

Ebert T (1986) Baroreflex responsiveness is maintained during isometric exercise in humans. J Appl Physiol 61:797–803

Ferrari G, Landolina M, Mantica M, Manfredini R, Schwartz P, Lotto A (1995) Baroreflex sensitivity, but not heart rate variability, is reduced in patients with life-threatening ventricular arrhythmias long after myocardial infarction. Am Heart J 130:473–480

Goldberger J, Challapalli S, Tung R, Parker M, Kadish A (2001) Relationship of heart rate variability to parasympathetic effect. Circulation 103:1977–1983

Iellamo F, Pizzinelli P, Massaro L, Raimondi G, Peruzzi G, Legramante JM (1999) Muscle metaboreflex contribution to sinus regulation during static exercise. Insights from spectral analysis of heart rate variability. Circulation 100:27–32

Jordan J, Shannon J, Grogan E, Biaggioni I, Robertson D (1999) A potent pressor response elicited by water drinking. Lancet 353:723

Jordan J, Shannon J, Black B, Ali Y, Farley M, Costa F, Diedrich A, Robertson R, Biaggioni I, Robertson D (2000) The pressor response to water drinking in humans: a sympathetic reflex? Circulation 101:504–509

Khurana R, Stetty A (1996) The value of isometric handgrip test-studies in various autonomic disorders. Clin Auton Res 6:211–218

Kjaer M, Secher N (1992) Neural influence on cardiovascular and endocrine responses to static exercise in humans. Sports Med 13:303–319

Lu C, Diedrich A, Tsung C, Paranjape S, Harris P, Byrne D, Jordan J, Robertson D (2003) Water ingestion as prophylaxis against syncope. Circulation 108:2660–2665

McHugh J, Keller N, Appalsamy M, Thomas S, Raj S, Diedrich A, Biaggioni I, Jordan J, Robertson D (2010) Portal osmopressor mechanism linked to transient receptor potential vanilloid 4 and blood pressure control. Hypertension 55:1433–1438

Pagani M, Lombardi F, Guzzeti S, Rimoldi O, Furlan R, Pizzinelli P, Sandrone G, Malfatto G, Dell'Orto S, Piccaluga E, Turiel M, Baselli G, Cerutti S, Malliani A (1986) Power spectral analysis of heart rate and arterial pressure variabilities as a marker of sympatho-vagal interaction in man and conscious dog. Circ Res 59:178–193

Routledge H, Chowdhary S, Coote J, Townend J (2002) Cardiac vagal response to water ingestion in normal human subjects. Clin Sci 103:157–162

Saeki Y, Atogami F, Takahashi K, Yoshizawa T (1997) Reflex control of autonomic function induced by posture change during the menstrual cycle. J Auton Nerv Syst 66:69–74

Sato N, Miyake S, Akatsu J, Kumashiro M (1995) Power spectral analysis of heart rate variability in healthy young women during the normal menstrual cycle. Psychosom Med 57:331–335

Schroeder C, Bush V, Norcliffe L, Luft F, Tank J, Jordan J, Hainsworth R (2002) Water drinking acutely improves orthostatic tolerance in healthy subjects. Circulation 106:2806–2811

Scott E, Greenwood J, Gilbey S, Stoker J, Mary D (2001) Water ingestion increases sympathetic vasoconstrictor discharge in normal human subjects. Clin Sci (Lond) 100:335–342

Seals D, Chase P, Taylor J (1988) Autonomic mediation of the pressor responses to isometric exercise in humans. J Appl Physiol 64:2190–2196

Seals D, Taylor J, Ng A, Esler M (1994) Exercise and aging: autonomic control of circulation. Med Sci Sports Exerc 16:568–576

Shannon J, Diedrich A, Biaggioni I, Tank J, Robertson R, Robertson D, Jordan J (2002) Water drinking as a treatment for orthostatic syndromes. Am J Med 112:355–360

Smith J, Stephens D, Winchester P, Williamson J (1997) Facial cooling-induced bradycardia: attenuating effect of central command at exercise onset. Med Sci Sports Exerc 29:320–325

Stewart J, Montgomery L, Glover J, Medow M (2007) Changes in regional blood volume and blood flow during static handgrip. Am J Physiol Heart Circ Physiol 293:H215–H223

Stratton JR, Halter JB, Hallstrom AP, Caldwell JH, Ritchie JL (1983) Comparative plasma catecholamine and hemodynamic responses to handgrip, cold pressure, and supine bicycle exercise testing in normal subjects. J Am Coll Cardiol 2:93–104