Journal of Functional Foods 71 (2020) 104017

Contents lists available at ScienceDirect

Journal of Functional Foods

journal homepage: www.elsevier.com/locate/jff

Short-term cardiovascular responses to ingestion of mineral water in healthy non-obese adults: Impact of mineral components

Cathriona Rosemary Monnard, Jean-Pierre Montani, Erik Konrad Grasser*

Department of Endocrinology, Metabolism and Cardiovascular System, University of Fribourg, 1700 Fribourg, Switzerland

ARTICLE INFO

Keywords:
Cardiac
Baroreflex
Natural product
Heart rate

ABSTRACT

Background: The role of mineral components in the hemodynamic response to water drinking is still elusive.
Methods: We conducted a randomized crossover study in 16 non-obese, healthy subjects (8 women) to investigate cardiovascular responses to water drinks differing in the mineral content. Continuous measurements included beat-to-beat blood pressure, electrocardiography derived RR-intervals, and impedance cardiography for a 30 min baseline period with a subsequent 60 min post-drink period.
Results: In response to mineral water, but not distilled water, we observed significant time effects with decreases in heart rate and double product and increases in baroreflex sensitivity. Moreover, we observed a significant treatment difference in average heart rate responses starting 30 min after ingestion, where mineral water decreased heart rate to a greater extent than distilled water ($p < 0.05$).
Conclusions: In young, healthy humans, drinking mineral water decreased heart rate in a time-dependent fashion, potentially due to its mineral properties.

1. Introduction

Water is recommended as the preferred beverage of choice for health for the general population (Popkin et al., 2006). Despite the focus on water drinking for health, the precise physiologic responses to water ingestion and the potential mechanisms underlying these responses have not yet been elucidated. Water drinking induces distinct hemodynamic responses that largely depend on the functionality of the autonomic nervous system. Indeed, patients suffering from disorders of autonomic failure substantially increase their blood pressure in response to water drinking (Cariga & Mathias, 2001; Jordan et al., 2000; Jordan, Shannon, Grogan, Biaggioni, & Robertson, 1999). However, this is not the case for healthy adults (Brown, Barberini, Dulloo, & Montani, 2005; Girona, Grasser, Dulloo, & Montani, 2014; Joannides, Moore, de la Gueronniere, & Thuillez, 1999; Jordan et al., 2000; Monnard & Grasser, 2017; Routledge, Chowdhary, Coote, & Townend, 2002; Scott, Greenwood, Gilbey, Stoker, & Mary, 2001) where an intact autonomic nervous system concomitantly activates sympathetic- and parasympathetic nerves in response to water drinking. In this context, water drinking induced parasympathetic related changes that resulted in an elevation of measures of cardiac vagal tone, which lead to a decrease in heart rate (Brown et al., 2005; Girona et al., 2014; Grasser, 2020; Monnard & Grasser, 2017; Routledge et al., 2002) with accompanying increases in baroreflex sensitivity (Brown et al., 2005; Girona et al., 2014; Monnard & Grasser, 2017) and high-frequency variability of RR-interval (Brown et al., 2005; Girona et al., 2014; Grasser, 2020; Monnard & Grasser, 2017; Routledge et al., 2002).

It has been observed that hemodynamic changes largely depend on the osmotic properties of the water drink, in which distilled water, but not a physiological saline water solution, affected markers for cardiac vagal tone in healthy young adults (Brown et al., 2005). Recently, evidence has been put forward that drinking cold- and room-, but not body-tempered tap water affected cardiac workload through a reduction in heart rate and double product that could be mediated by augmented measures of cardiac vagal tone markers (Girona et al., 2014; Monnard & Grasser, 2017). To the best of our knowledge, we are only aware of a single study where acute cardiovascular changes in response to a mineral water drink were investigated (Callegaro et al., 2007), although this study lacked a negative control. Therefore, it remains to be seen whether mineral components contained in a mineral water drink play a role in acute cardiovascular responses to water ingestion in healthy humans.

In order to gain a greater understanding of the potential contribution of mineral water and its mineral components to the cardiovascular and autonomic responses to water drinking, we recruited 16 non-obese, healthy adults and measured cardiovascular changes in response to (*i*) a

* Corresponding author at: Department of Endocrinology, Metabolism and Cardiovascular System, University of Fribourg, Chemin du Musée 5, 1700 Fribourg, Switzerland.
E-mail address: erikkonrad.grasser@unifr.ch (E.K. Grasser).

https://doi.org/10.1016/j.jff.2020.104017
Received 12 October 2019; Received in revised form 10 May 2020; Accepted 10 May 2020
Available online 21 May 2020

common commercially available mineral water drink (with a stable mineral content) and to (*ii*) a distilled water control by using a randomized crossover design.

2. Materials and methods

2.1. Subjects

Sixteen (8 women) healthy, young (all: 24.8 ± 0.8 years; men: 24.1 ± 1.1 years and women: 25.4 ± 1.1 years; $p = 0.42$) subjects were recruited from among local students and their friends. The mean height of the participants was 171 ± 3 cm (men: 182 ± 2 cm and women: 161 ± 2 cm, $p < 0.005$), body weight was 76 ± 3 kg (men: 85 ± 3 kg and women: 66 ± 4 kg, $p < 0.005$), and body mass index was 25.5 ± 0.6 kg·m^{-2} (men: 25.8 ± 0.6 kg·m^{-2} and women: 25.2 ± 1.2 kg·m^{-2}, $p = 0.67$). All of the test subjects were non-obese (body mass index < 30 kg·m^{-2}) with normal resting blood pressure and normal resting heart rate. None of the subjects had any diseases or were taking any medication affecting cardiovascular regulation. All participants fasted (no food or water) for ≥ 12 h and abstained from alcohol, smoking and caffeine, as well as from vigorous exercise for 24 h prior to each test and were advised not to change their dietary habits between the tests. This study was conducted according to the guidelines laid down by the *Declaration of Helsinki* and all procedures involving human subjects were approved by the Institutional ethical review board for human experiments (protocol 105/15). Written informed consent was obtained from all subjects.

2.2. Study design

All studies started between 08:00 and 08:30 in an air-conditioned (temperature 22 °C) and quiet laboratory solely dedicated for human physiological experiments, with subjects at thermal comfort. Every test subject attended two separate experimental sessions (separated by at least 2 days) according to a randomized crossover design, where women were studied in their follicular phase (day 1–14 of the menstrual cycle; determined as the week of menstruation plus the following week). Randomization was performed using a random sequence generator (https://www.randomizer.org/) where the sessions order was determined before the start of the study. At each experimental session, cardiovascular responses to one of two drinks were monitored. The content of the drinks tested were as follows: (*i*) still mineral water from a common commercially available drink (*Evian*® containing 360 mg·L^{-1} bicarbonate, 6.5 mg·L^{-1} sodium, 80 mg·L^{-1} calcium, 26 mg·L^{-1} magnesium, 1 mg·L^{-1} potassium, 3.8 mg·L^{-1} chloride, and 12.6 mg·L^{-1} sulfate. All mineral content data were accessed from the list of ingredients that was attached to each bottle *Evian*® still mineral water, and (*ii*) distilled water (water distillation unit, Model GFL 2012, Gesellschaft für Labortechnik mbH, Burgwedel, Germany). The measured osmolality of the mineral water drink was 7.97 mOsm·L^{-1} (average from three different mineral water samples at which each sample comprised of the average of 10 measurements by using a *Fiske 110 Osmometer*, U.S.A.) and calculated osmolality was 7.94 mOsm·L^{-1}. Distilled water presented a measured osmolality of 0 mmol·L^{-1} (average from three different distilled water samples at which each sample comprised of the average of 10 measurements by using a *Fiske 110 Osmometer*, U.S.A.). Each drink volume was 500 mL (chosen based on a previous study that investigated cardiovascular responses to water ingestion (Girona et al., 2014)), served at room temperature, and was drunk at a convenient pace over 4 min. The subjects were blinded to the order of the drinks.

On arrival at the laboratory, subjects were asked to empty their bladders if necessary and to sit in a comfortable armchair. All subjects wore light clothing consisting of a t-shirt and trousers. The equipment was then connected and the test subject's upper body was covered with a light blanket. After waiting for a period of 20–30 min to attain cardiovascular stability, recordings were initiated with a 30 min baseline after which the subject ingested one of the test drinks over a period of 4 min, which has previously been shown to allow enough time for subjects to drink a similar volume at a convenient pace (Girona et al., 2014; Miles-Chan, Charrière, Grasser, Dulloo, & Montani, 2015; Monnard & Grasser, 2017). Then, post-drink cardiovascular and autonomic recordings continued for another 60 min. Throughout the investigation subjects were allowed to watch neutral films/documentaries to avoid boredom.

2.3. Hemodynamics

A Task Force Monitor (CNSystems, Medizintechnik, Graz, Austria) was used to perform cardiovascular and autonomic recordings, and data were sampled at a rate of 1000 Hz (Girona et al., 2014). Continuous blood pressure was monitored using the Penaz principle from either the index or middle finger (automatically finger switch every 30 min) of the right hand and was calibrated to oscillometric brachial blood pressure measurements on the contralateral arm (Girona et al., 2014). The right hand with the continuous blood pressure cuff rested on a ductile pillow, which was positioned at heart level on a height adjustable table (Girona et al., 2014). Electrocardiography electrodes were positioned together with upper arm and finger blood pressure cuffs (Girona et al., 2014). Baroreflex sensitivity was determined from spontaneous fluctuations in blood pressure and cardiac interval using the sequence technique (Girona et al., 2014).

2.4. Data and statistical analysis

Beat-to-beat values for cardiac interval (RR-interval), systolic blood pressure, diastolic blood pressure, double product, cardiac output, total peripheral resistance, and baroreflex sensitivity were averaged every 10 min during the 30 min baseline period and within the 60 min post-drink period. Mean blood pressure was calculated as the result of diastolic blood pressure + 1/3 (systolic blood pressure – diastolic blood pressure) and heart rate was assessed from the appropriate RR-interval. Double product, which provides information about cardiac oxygen demand (Schutte et al., 2013), was calculated as heart rate × systolic blood pressure, cardiac output as heart rate × stroke volume, and total peripheral resistance as mean blood pressure divided by cardiac output.

All values reported in this study are presented as means ± standard error of the means. Two-way repeated measures *ANOVA* with *Bonferroni*'s post-hoc analysis was used with condition and time as within subject factors to determine the effect of condition (treatments, i.e. mineral water and distilled water) and time on the measured variables, as well as any potential interaction effect (condition × time). Where time effects were observed in the two-way repeated measures *ANOVA*, one-way repeated measures *ANOVA* with *Dunnett's* multiple comparisons post hoc testing was used to determine where these differences resided (Figs. 1-3, left panels). Whenever appropriate, we used a paired *t*-test to compare between treatments (Figs. 1-3, right panels). For all tests, significance was set at $p \leq 0.05$.

3. Results

Baseline cardiovascular (heart rate, baroreflex sensitivity, systolic blood pressure, diastolic blood pressure, double product, cardiac output, and total peripheral resistance) parameters were similar between treatment and control (Table 1). No adverse effects were observed in response to treatment or control in any subject during the observational period.

3.1. Cardiovascular responses

Overall, two-way repeated measures ANOVA did not reveal any significant difference between treatments for all investigated

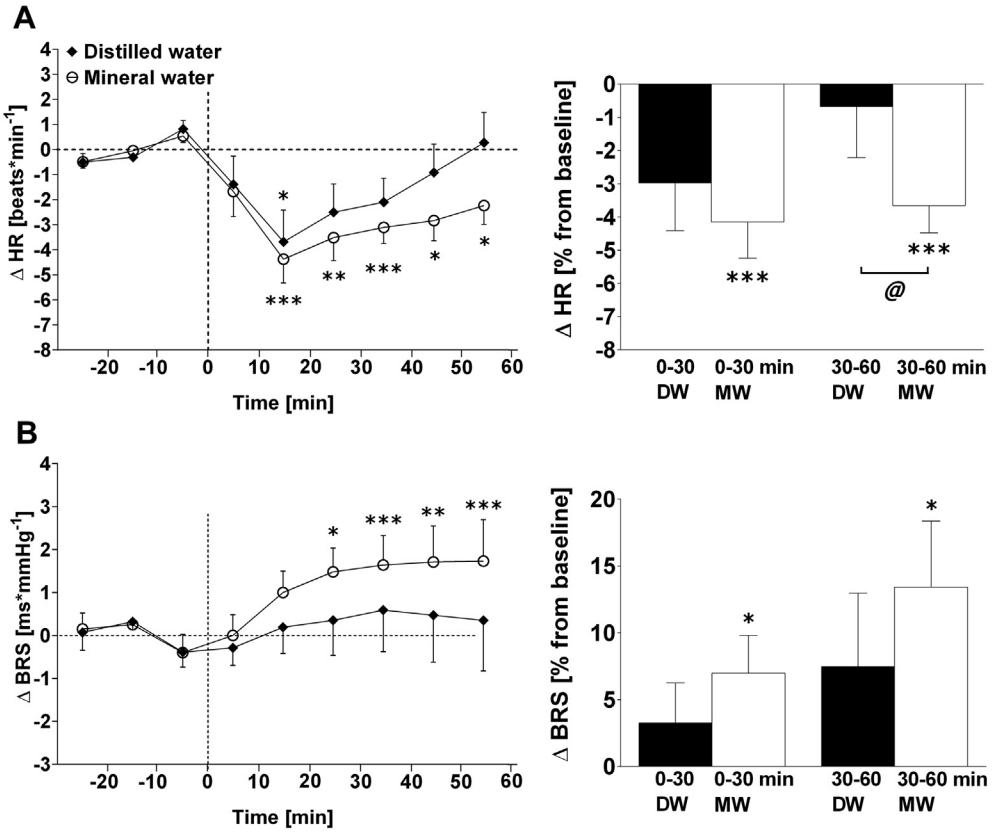

Fig. 1. Changes in heart rate (HR) (Fig. 1**A**) and baroreflex sensitivity (BRS) (Fig. 1**B**) from a 30-min baseline in 16 subjects drinking either distilled water (DW) or mineral water (MW). **Left panels**: Changes from baseline in absolute values with each symbol representing a 10-min time period (time 0 indicates resumption of the recordings after the 4 min drink period). **Right panels**: Percentage changes from baseline averaged over the 0–30 and 30–60 min post-drink period, respectively. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.005$, statistically significant differences from baseline values (left and right panels). $^{@}p < 0.05$, statistically significant difference between drink conditions (right panel). Data are presented as means ± standard error of the means.

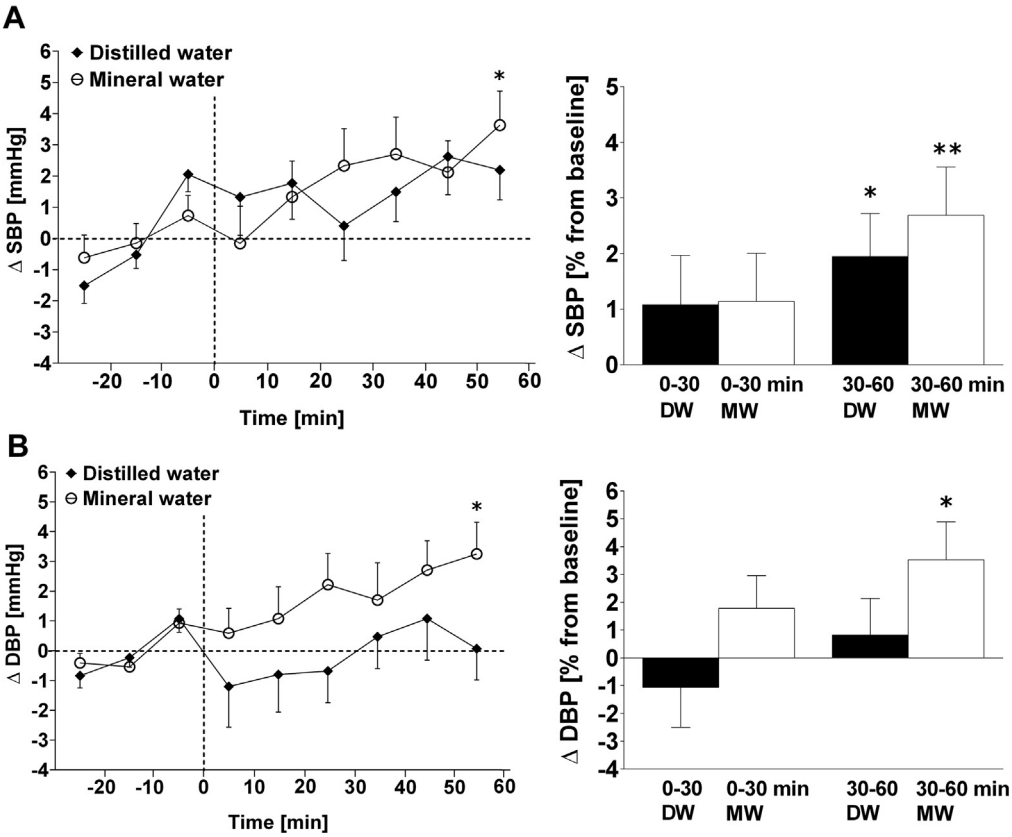

Fig. 2. Changes in systolic blood pressure (SBP) (**A**) and diastolic blood pressure (DBP) (**B**) from a 30-min baseline in 16 subjects drinking either distilled water (DW) or mineral water (MW). **Left panels**: Changes from baseline in absolute values with each symbol representing a 10-min time period (time 0 indicates resumption of the recordings after the 4 min drink period). **Right panels**: Percentage changes from baseline averaged over the 0–30 and 30–60 min post-drink period, respectively. $^{*}p < 0.05$, $^{**}p < 0.01$ and $^{***}p < 0.005$, statistically significant differences from baseline values (left and right panels). Data are presented as means ± standard error of the means.

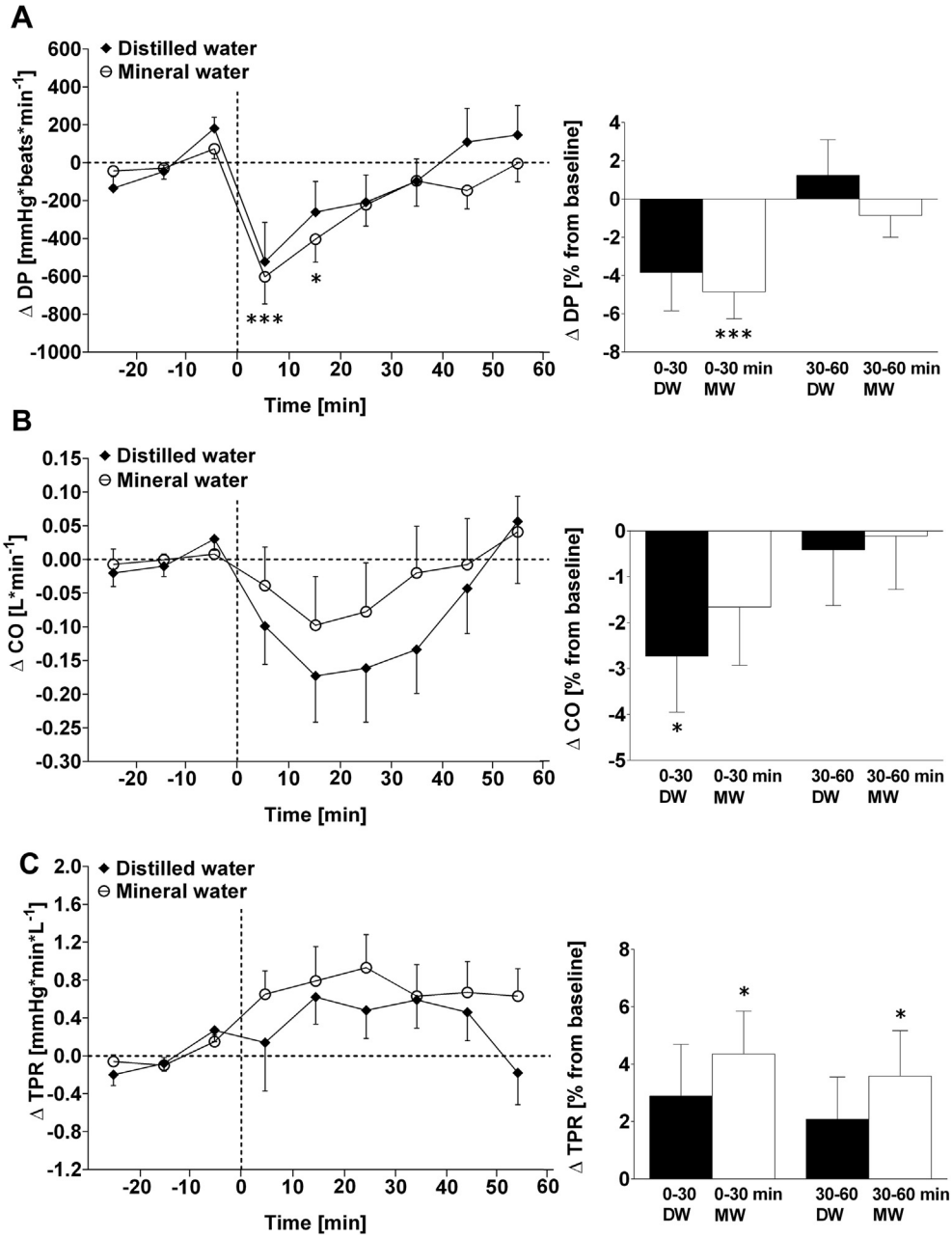

Fig. 3. Changes in double product (DP) (**A**), cardiac output (CO) (**B**), and total peripheral resistance (TPR) (**C**) from a 30-min baseline in 16 subjects drinking either distilled water (DW) or mineral water (MW). **Left panels**: Changes from baseline in absolute values with each symbol representing a 10-min time period (time 0 indicates resumption of the recordings after the 4 min drink period). **Right panels**: Percentage changes from baseline averaged over the 0–30 and 30–60 min post-drink period, respectively. $*p < 0.05$, $**p < 0.01$ and $***p < 0.005$, statistically significant differences from baseline values (left and right panels). Data are presented as means ± standard error of the means.

Table 1
Baseline cardiovascular and autonomic characteristics for 16 (8 women) young, healthy subjects.

	Baseline all Distilled water	Baseline all Mineral water
Heart rate, beats·min^{-1}	71 ± 2	71 ± 2
Baroreflex sensitivity, ms·mmHg^{-1}	20.6 ± 2.5	18.5 ± 2.1
Systolic blood pressure, mmHg	116 ± 3	114 ± 3
Diastolic blood pressure, mmHg	77 ± 2	74 ± 2
Double product, beats·min^{-1} ·mmHg	8088 ± 264	8045 ± 290
Cardiac output, L·min^{-1}	5.0 ± 0.2	4.9 ± 0.2
Total peripheral resistance, mmHg·min·L^{-1}	18.3 ± 0.6	18.1 ± 0.6

Averaged responses over 30 min continuous measurements before drinking 500 mL of distilled water or mineral water using a randomized crossover study design. No significant differences were observed between the drink conditions at baseline (all $p > 0.05$). All values are presented as means ± standard error of the means.

cardiovascular responses (all $p > 0.05$).

Significant time course changes for heart rate were observed compared to baseline values in response to both mineral and distilled water. For both drinks, heart rate was lowest within the first 20 min post-drink (distilled water −3.7 ± 1.3 beats·min^{-1}, $p = 0.048$; mineral water: −4.4 ± 0.9 beats·min^{-1}, $p < 0.005$). However, and in response to mineral water, but not distilled water, heart rate remained significantly below baseline values over the entire post-drink period (Fig. 1 A, left panel), which can be best seen by a significant difference between treatments from 30 to 60 min post-drink (−0.7 ± 1.5% vs −3.7 ± 0.8%, $p = 0.04$) (Fig. 1 A, right panel). Furthermore, mineral, but not distilled water gradually increased baroreflex sensitivity over time with a peak response around 60 min post-drink (+1.7 ± 1.0 ms·mmHg^{-1}, $p < 0.005$) (Fig. 1 B, left panel). In response to mineral, but not to distilled water average percentage changes for baroreflex sensitivity over 30 min (+7.0 ± 2.8%, $p = 0.03$) and 60 min (+13.4 ± 4.9%, $p = 0.02$) were significantly higher compared to baseline values (Fig. 1 B, right panel).

Distilled and mineral water affected systolic blood pressure similarly by inducing a slow and steady increase over time with peak responses between 50 and 60 min post-drink (distilled water: +2.6 ± 1.2 mmHg, $p = 0.19$; mineral water: +3.6 ± 1.1 mmHg, $p = 0.02$). However, mineral, but not distilled water increased diastolic blood pressure over time, peaking around 60 min post-drink (+3.3 ± 1.1 mmHg, $p = 0.04$) (Fig. 2 A and B, left and right panels).

Ingestion of mineral water significantly decreased double product over the first 30 min post drink (−4.9 ± 1.4%, $p < 0.005$) and increased total peripheral resistance as averaged percentage change from baseline values over 0 to 30 min (+4.4 ± 1.5%, $p = 0.01$), as well as over 30 to 60 min post-drink (+3.6 ± 1.6%, $p = 0.04$) (Fig. 3 A and C, right panels). Distilled, but not mineral water, decreased cardiac output (−2.7 ± 1.2%, $p = 0.04$) within the first 30 min post drink (Fig. 3 B, right panel).

4. Discussion

This study investigated, using a randomized crossover design, cardiovascular changes in non-obese, healthy adults in response to a commercially available mineral water drink and compared those responses to a distilled water control. In response to mineral water, but not distilled water, we observed significant time effects for heart rate, baroreflex sensitivity, diastolic blood pressure, and double product. Moreover, we observed a significant treatment difference in average heart rate responses starting 30 min after ingestion where mineral water decreased heart rate to a greater extent than distilled water. Indeed, as shown in Fig. 1A, both treatments, i.e. mineral and distilled water, significantly decreased heart rate over the first 30 min after ingestion to almost the same magnitude, whilst for the subsequent 30 min, for mineral, but not distilled water, heart rate remained significantly below baseline values. In addition, there was a trend for baroreflex sensitivity to be higher with mineral water (Fig. 1B). Taken together, our mineral water drink decreased heart rate in a time-dependent fashion and tended to increase baroreflex sensitivity to a greater extent than distilled water.

Resting heart rate is known to affect myocardial function (Fox et al., 2007), such that elevated resting heart rate increases the risk for cardiovascular diseases (Fox et al., 2008; Palatini, 2009; Reil et al., 2011). Moreover, in postmyocardial infarction patients, low baroreflex sensitivity is considered a cardiovascular risk factor (La Rovere et al., 2001; La Rovere, Bigger, Marcus, Mortara, & Schwartz, 1998), an observation also seen in low-risk patients (De Ferrari et al., 2007). Consequently, interventions or treatments that would reduce resting heart rate and/or increase baroreflex sensitivity without concomitant negative side effects are highly desirable. In this context, our laboratory (Girona et al., 2014; Monnard & Grasser, 2017), and others (Routledge et al., 2002), provided evidence that in young, normal weight subjects, a tap water drink reduces resting heart rate and increases baroreflex sensitivity. These changes could be due to the hypoosmotic properties (Brown et al., 2005) and/or differences in the temperature of the water drink (Girona et al., 2014). However, little is known about the role of minerals contained in a mineral water drink in modulating cardiovascular responses.

4.1. Acute heart rate responses to drinking mineral water (0 to 30 min post-drink)

Both water drinks in our study decreased heart rate to almost the same extent for the first 30 min after ingestion, which could be due to vagal branch activation of the autonomic nervous system. In our experiment, the serving temperature for treatment and control drinks (~22 °C, respectively) was substantially lower compared to gastrointestinal temperatures (between 36 and 37 °C, Monnard et al., 2017). Given that the nadir of our observed treatment responses to heart rate was around 20 min after drink ingestion, and considering the half-time for gastric emptying of a saline solution (approximately 12 min in a fasted state in humans (Reinus & Simon, 2014), a drink temperature-induced activation of transient receptor potential channels within the splanchnic area seems possible. Our findings are in line with recent work from our laboratory where cold- and room-tempered tap water (3 °C and 22 °C, respectively), but not body-tempered tap water (37 °C), decreased heart rate significantly. Moreover, the human stomach offers a mere 0.053 m^2 of absolute surface area, which is rather insignificant in terms of absorption when compared to 200 m^2 for the small intestine (De Sesso & Jacobson, 2001). Therefore, it seems reasonable to explain, at least partly, initial heart rate responses to water ingestion by drink temperature-related activations of temperature sensing channels located in the splanchnic area. Since heart rate responses to ingestion of mineral water and distilled water followed a very similar time course within the first 30 min post-drink, it seems likely that drink temperature, but not mineral content accounted for observed heart rate responses.

4.2. Preserved heart rate responses to drinking mineral water (30 to 60 min post-drink)

Our main finding was that in response to mineral water, heart rate remained significantly below baseline values over 60 min after its ingestion, whilst in response to distilled water heart rate returned back to baseline values starting around 30 min post-drink. One potential explanation for this observation might be due to concurrent changes in blood pressure, which, in turn, may affect heart rate. However, and by performing a regression analysis, we were not able to find any significant correlation of delta heart rate responses with systolic and diastolic blood pressure changes (all p between 0.3 and 0.9 over 0–30, 30–60, and 0–60 min periods, respectively). Therefore, the results from the present study do support a direct and preserved effect of mineral water on heart rate that is independent of changes in blood pressure.

Another potential explanation for a preserved heart rate response to mineral water could be due to mineral and trace elements contained in our mineral water drink, which were not present in the distilled water control. It could be speculated that the small difference in osmolality between our treatments (i.e. ~8 mOsm/L for the mineral water drink versus 0 mOsm/L for distilled water) contributed, at least in part, for the preserved heart rate response to mineral water. This contention is further substantiated by knowledge of the maximum capacity of water absorption in the small intestine, which is about 15 mL/min (Leiper, 2015). This, in turn, suggests at least > 40 min of gradual absorption in response to our drink volume of 500 mL when transit times by the stomach were taken into account. Therefore, and because both of our study drinks had similar drink temperatures (~22 °C), which were warmed up to core temperature levels, it is conceivable that differences in mineral and trace elements were, at least partly, responsible for differences in preserved heart rate responses to mineral water. On the other hand, an earlier study provided evidence that an isotonic saline drink did not affect heart rate responses at all (Brown et al., 2005), thus it is suggestible that the combination of low osmolality with some other minerals in small quantities and varying in sodium chloride potentially triggers heart responses. However, because of our observational study design, we can only speculate about potential mineral components, which could explain this contention.

In this context, acid-sensitive ion channels can provide one potential alternative molecular physiological explanation for distinct autonomic changes in response to our mineral water drink. Among these, vanilloid transient receptor potential channel V1 (TRPV1) and acid-sensing ion channels have been most intensely investigated (Holzer, 2009). However, TRPV1 and TRPV4 channels are activated only by acidosis with a pH below 6 (Holzer, 2009; Suzuki, Mizuno, Kodaira, & Imai, 2003), making them unlikely candidates to convey our observed heart rate responses. On the other hand, acid-sensing ion channels are known to sense even small changes in extracellular pH (Holzer, 2009) and are

expressed by the peripheral axons of vagal and spinal afferent neurons (Holzer, 2015). Indeed, our mineral water drink was relatively high in bicarbonate, which contributed to ~54% of the drink's total osmolality. Therefore, although highly speculative, the difference in bicarbonate between mineral water and distilled water could be a potential explanation for our findings with regard to heart rate.

To the best of our knowledge, we are not aware of any study that has compared the hemodynamic response to mineral water versus distilled water in the same individual as in the current study. This novel aspect of our study allowed us to test for subtle changes between the drinks, which would not have been possible by looking at different populations. Nonetheless, the current study has some caveats: *Firstly*, although the study included both genders, the sample size was too small to investigate potential gender differences. Therefore, future studies are required with sufficient numbers of male and female subjects to investigate whether gender differences exist in the response to mineral water. *Secondly*, given that this study was not a chronic interventional study, which we acknowledge as a limitation to our test design, we cannot conclude that mineral water would exert a beneficial effect on cardiovascular morbidity or mortality. However, the greater decrease in heart rate and the slightly greater increase in baroreflex sensitivity could be considered as beneficial cardiovascular effects.

In conclusion, we investigated, in healthy, non-obese humans, cardiovascular changes in response to a low osmolality mineral water drink and compared those changes to a distilled water control. We observed in response to mineral and distilled water a similar time course for heart rate responses over the first 30 min after ingestion of each, which resulted in significantly lower heart rates. However, heart rate responses over the subsequent 30 min post-drink clearly differed between the two drinks. In this context, mineral, but not distilled water maintained heart rate responses significantly below baseline values. Because mineral and distilled water were ingested both at room temperature, minerals and trace elements contained in the mineral water drink might be involved in these observations. Taken together, our study results provide evidence that in young and healthy subjects a commercially available still mineral water drink reduces cardiac workload in a time-dependent fashion, as suggested by short-term reductions in heart rate and double product. However, our study design and its results do not qualify for making a statement or a conclusion about long-term health benefits. Nevertheless, further studies are warranted to investigate prospectively potential beneficial effects of drinking mineral water over a longer period of time.

Fundings

This work was financed by intramural funding.

Disclosures

The authors declare no potential conflicts of interest, financial or otherwise, with respect to this manuscript.

Ethics statements file

This study was conducted according to the guidelines laid down by the *Declaration of Helsinki* and all procedures involving human subjects were approved by the institute's ethical review board. Written informed consent was obtained from all subjects.

CRediT authorship contribution statement

Cathriona Rosemary Monnard: Formal analysis, Writing - review & editing. **Jean-Pierre Montani:** Conceptualization, Methodology, Writing - review & editing, Supervision. **Erik Konrad Grasser:** Formal analysis, Writing - original draft, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

Brown, C. M., Barberini, L., Dulloo, A. G., & Montani, J.-P. (2005). Cardiovascular responses to water drinking: Does osmolality play a role? *American Journal of Physiology – Regulatory, Integrative and Comparative Physiology, 289*, R1687–R1692.

Callegaro, C. C., Moraes, R. S., Negrão, C. E., Trombetta, I. C., Rondon, M. U., ... Ribeiro, J. P. (2007). Acute water ingestion increases arterial blood pressure in hypertensive and normotensive subjects. *Journal of Human Hypertension, 21*, 564–570.

Cariga, P., & Mathias, C. J. (2001). Haemodynamics of the pressor effect of oral water in human sympathetic denervation due to autonomic failure. *Clinical Science (London), 101*, 313–319.

De Ferrari, G. M., Sanzo, A., Bertoletti, A., Specchia, G., Vanoli, E., & Schwartz, P. J. (2007). Baroreflex sensitivity predicts long-term cardiovascular mortality after myocardial infarction even in patients with preserved left ventricular function. *Journal of the American College of Cardiology, 50*, 2285–2290.

De Sesso, J. M., & Jacobson, C. F. (2001). Anatomical and physiological parameters affecting gastrointestinal absorption in humans and rats. *Food and Chemical Toxicology, 39*, 209–228.

Fox, K., Borer, J. S., Camm, A. J., Danchin, N., Ferrari, R., ... Heart Rate Working Group (2007). Resting heart rate in cardiovascular disease. *Journal of the American College of Cardiology, 50*, 823–830.

Fox, K., Ford, I., Steg, P. G., Tendera, M., Robertson, M., & Ferrari, R. (2008). Heart rate as a prognostic risk factor in patients with coronary artery disease and left-ventricular systolic dysfunction (BEAUTIFUL): A subgroup analysis of a randomised controlled trial. *Lancet, 372*, 817–821.

Girona, M., Grasser, E. K., Dulloo, A. G., & Montani, J.-P. (2014). Cardiovascular and metabolic responses to tap water ingestion in young humans: Does the water temperature matter? *Acta Physiologica (Oxford), 211*, 358–370.

Grasser, E. K. (2020). Dose-dependent heart rate responses to drinking water: a randomized crossover study in young, non-obese males. Clinical Autonomic Research (epub ahead of print).

Holzer, P. (2009). Acid-sensitive ion channels and receptors. *Handbook of Experimental Pharmacology, 194*, 283–332.

Holzer, P. (2015). Acid-sensing ion channels in gastrointestinal function. *Neuropharmacology, 94*, 72–79.

Joannides, R., Moore, N., de la Gueronniere, V., & Thuillez, C. (1999). Effect of water on arteries. *Lancet, 354*, 516.

Jordan, J., Shannon, J. R., Black, B. K., Ali, Y., Farley, M., ... Robertson, D. (2000). The pressor response to water drinking in humans: A sympathetic reflex? *Circulation, 101*, 504–509.

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

La Rovere, M. T., Bigger, J. T., Marcus, F., Mortara, A., & Schwartz, P. J. (1998). Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. *Lancet, 351*, 478–484.

La Rovere, M. T., Pinna, G. D., Hohnloser, S. H., Marcus, F. I., Mortara, A., ATRAMI Investigators, ... Autonomic Tone and Reflexes After Myocardial Infarction (2001). Baroreflex sensitivity and heart rate variability in the identification of patients at risk for life-threatening arrhythmias: Implications for clinical trials. *Circulation, 103*, 2072–2077.

Leiper, J. B. (2015). Fate of ingested fluids: Factors affecting gastric emptying and intestinal absorption of beverages in humans. *Nutrition Reviews, 73*, 57–72.

Miles-Chan, J. L., Charrière, N., Grasser, E. K., Dulloo, A. G., & Montani, J.-P. (2015). The blood pressure-elevating effect of Red Bull energy drink is mimicked by caffeine but through different hemodynamic pathways. *Physiological Reports, 3* e12290–e12290.

Monnard, C. R., Fares, E. J., Calonne, J., Miles-Chan, J. L., Montani, J.-P., ... Dulloo, A. G. (2017). Issues in continuous 24-h core body temperature monitoring in humans using an ingestible capsule telemetric sensor. *Frontiers in Endocrinology (Lausanne), 8*, 130.

Monnard, C. R., & Grasser, E. K. (2017). Water ingestion decreases cardiac workload time-dependent in healthy adults with no effect of gender. *Scientific Reports, 7*, 7939.

Palatini, P. (2009). Elevated heart rate: A "new" cardiovascular risk factor? *Progress in Cardiovascular Diseases, 52*, 1–5.

Popkin, B. M., Armstrong, L. E., Bray, G. M., Caballero, B., Frei, B., & Willett, W. C. (2006). A new proposed guidance system for beverage consumption in the United States. *American Journal of Clinical Nutrition, 83*, 529–542.

Reil, J. C., Custodis, F., Swedberg, K., Komajda, M., Borer, J. S., ... Böhm, M. (2011). Heart rate reduction in cardiovascular disease and therapy. *Clinical Research in Cardiology, 100*, 11–19.

Reinus, J. F., & Simon, D. (Eds.). (2014). *Gastrointestinal anatomy and physiology: the essentials*. Wiley Blackwell: John Wiley & Sons Ltd.

Routledge, H. C., Chowdhary, S., Coote, J. H., & Townend, J. N. (2002). Cardiac vagal response to water ingestion in normal human subjects. *Clinical Science (London), 103*, 157–162.

Schutte, R., Thijs, L., Asayama, K., Boggia, J., Li, Y., ... Staessen, J. A. (2013). Double product reflects the predictive power of systolic pressure in the general population: Evidence from 9,937 participants. *American Journal of Hypertension, 26*, 665–672.

Scott, E. M., Greenwood, J. P., Gilbey, S. G., Stoker, J. B., & Mary, D. A. (2001). Water ingestion increases sympathetic vasoconstrictor discharge in normal human subjects. *Clinical Science (London), 100*, 335–342.

Suzuki, M., Mizuno, A., Kodaira, K., & Imai, M. (2003). Impaired pressure sensation in mice lacking TRPV4. *Journal of Biological Chemistry, 278*, 22664–22668.