Cardiovascular responses to water drinking: does osmolality play a role?

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Brown, Clive M., Luc Barberini, Abdul G. Dulloo, and Jean-Pierre Montani. Cardiovascular responses to water drinking: does osmolality play a role? Am J Physiol Regul Integr Comp Physiol 289: R1687–R1692, 2005. First published July 21, 2005; doi:10.1152/ajpregu.00205.2005.—Water drinking activates the autonomic nervous system and induces acute hemodynamic changes. The actual stimulus for these effects is undetermined but might be related to either gastric distension or to osmotic factors. In the present study, we tested whether the cardiovascular responses to water drinking are related to water’s relative hypoosmolality. Therefore, we compared the cardiovascular effects of a water drink (7.5 ml/kg body wt) with an identical volume of a physiological (0.9%) saline solution in nine healthy subjects (6 male, 3 female, aged 26 ± 2 years), while continuously monitoring beat-to-beat blood pressure (finger plethysmography), cardiac intervals (electrocardiography), and cardiac output (thoracic impedance). Total peripheral resistance was calculated as mean blood pressure/cardiac output.

Cardiac interval variability (high-frequency power) was assessed by spectral analysis as an index of cardiac vagal tone. Baroreceptor sensitivity was evaluated using the sequence technique. Drinking water, but not saline, decreased heart rate (P = 0.01) and increased total peripheral resistance (P < 0.01), high-frequency cardiac interval variability (P = 0.03), and baroreceptor sensitivity (P = 0.01). Neither water nor saline substantially increased blood pressure. These responses suggest that water drinking simultaneously increases sympathetic vasoconstrictor activity and cardiac vagal tone. That these effects were absent after drinking physiological saline indicate that the cardiovascular responses to water drinking are influenced by its hypoosmotic properties.

baroreceptors; blood pressure; cardiac output; heart rate; autonomic nervous system

THE SIMPLE AND ESSENTIAL ACT of drinking water has several effects on human cardiovascular autonomic regulation. Ingestion of about half a liter of water augments sympathetic vasoconstrictor tone, as shown by increases in muscle sympathetic nerve activity, calf vascular resistance, and plasma norepinephrine levels (8, 22). In young healthy persons, the sympathetic activation after water drinking causes little or no change in blood pressure (8, 21, 22). Healthy elderly individuals show a moderate pressor response of ~11 mmHg after drinking water (8). However, in patients with autonomic failure, water drinking can substantially increase blood pressure by more than 30 mmHg for an hour or more (4, 8). There is some controversy as to the mechanism of this pressor effect. Mathias and colleagues (4, 13, 14) argue that the time course of the response is inconsistent with an autonomic reflex and that other mechanisms, for example, an intravascular volume expansion, are responsible. In contrast, Jordan et al. (8) favor a sympathetic reflex, since ganglionic blockade almost completely abolishes the pressor effect of water in autonomic failure patients. Clinically, water drinking might lead to potentially dangerous blood pressure elevations, especially in patients with supine hypertension or with poor autonomic regulation (7). On the other hand, water drinking improves orthostatic tolerance (11, 21) and might even have therapeutic benefits in patients with orthostatic syncope or postprandial hypotension (25).

As well as activating the sympathetic nervous system, water drinking also enhances cardiovagal tone in young healthy subjects. This is demonstrated by a reduction in heart rate and an increase in heart rate variability (20). It has been suggested that the cardiovagal activation buffers the pressor effect of water in young subjects and that the blood pressure rise in older subjects and patients with autonomic failure might be explained by an impaired buffering capacity (20).

The actual stimulus that elicits the autonomic responses to water drinking is so far undetermined. One possibility is that the responses are triggered by gastric distension, which has been shown to increase sympathetic activity and blood pressure (19). However, in contrast to water drinking, stomach distension also increases heart rate (19). Another possibility is that the responses to water drinking are influenced by water’s hypoosmotic properties. This could be either through changes in overall plasma osmolality or by local stimulation of osmoreceptive nerves, perhaps in the gut or the portal circulation. However, the acute effects of osmotic stimulation on cardiovascular regulation have not been well studied in humans. Specifically, it is not known how ingesting drinks of differing osmolality can influence blood pressure, heart rate, cardiac output, vascular resistance, or the underlying autonomic modulation, as reflected by heart rate variability and baroreflex sensitivity.

The aim of the present work was to determine, in a comprehensive study, whether the hypoosmotic properties of water play a role in the cardiovascular responses to drinking in normal subjects. Therefore, in a series of healthy young individuals, we compared the beat-to-beat cardiovascular responses and autonomic modulation to a distilled water drink with the responses to a physiological (0.9%) saline drink.

MATERIALS AND METHODS

Subjects. We studied nine healthy volunteers (6 male, 3 female), aged 20–34 (mean 26 ± 2 years). Their height was 175 ± 3 cm, and their weight was 69 ± 2 kg. None of the subjects had any diseases or were taking any medication affecting the cardiovascular or autonomic systems. Each participant was requested to avoid heavy exercise for at least 24 h before the experiment and to have nothing to eat or drink on the morning of the measurement. Subjects were asked to empty their bladders just before the experiment. Written informed consent was obtained from each subject. All procedures were approved by the

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University of Fribourg review board for human subjects and complied with the Declaration of Helsinki.

Protocol. Studies were carried out in the morning in a temperature-controlled quiet laboratory. Each subject attended two experimental sessions according to a randomized cross-over design. Subjects were studied in a seated position. The instruments for cardiovascular monitoring were attached, and the recording started once the signals had stabilized. After a 20-min control period, the subjects drank 7.5 ml/kg body wt (mean volume $517 \pm 15$ ml) of either distilled water or a 0.9% saline solution. The drink was served at room temperature (21°C) and was ingested over a period of 3 min. Before the measurements, subjects were blinded as to the order of the drinks. Cardiovascular monitoring was continued for a further 60 min after the drink.

Noninvasive cardiovascular recordings were performed using a task force monitor (CNSystems, Medizintechnik, Graz, Austria) with data sampled at a rate of 1,000 data points per second. Cardiac intervals (and their reciprocal, heart rate) were recorded by ECG. Continuous blood pressure was recorded from the middle finger of the right hand using the vascular unloading technique and was calibrated to oscillometric brachial blood pressure measurements on the contralateral arm. Thoracic impedance was recorded using band electrodes, one placed on the back of the neck and two parallel electrodes placed on the lateral sides of the thorax at the level of the xiphoid process. Cardiac stroke volume was derived on a beat-to-beat basis from the impedance cardiogram (10).

Time control experiments undertaken in four healthy subjects over 80 min with the same experimental setup but with no drink showed that the maximum spontaneous change in heart rate, blood pressure, cardiac output, and total peripheral resistance over the last 60 min was less than 3% from the initial 20-min value.

Time and frequency domain analysis. The beat-to-beat values of cardiac interval, blood pressure (systolic, mean, and diastolic), and stroke volume were resampled at a rate of 5.12 Hz to provide time series with equidistant data points. Cardiac output was calculated as the product of stroke volume and heart rate. Total peripheral resistance was calculated as mean blood pressure divided by cardiac output.

Cardiac interval variability was evaluated by power spectral analysis (27). Data sets of 2,048 points (400 s) were analyzed by Fast Fourier transformation using a Hamming window. For each data set, spectral power was obtained in the low-frequency (LF; 0.03–0.15 Hz) and high-frequency (HF; 0.15–0.40 Hz) ranges.

Cardiac baroreflex sensitivity was assessed from spontaneous fluctuations in systolic blood pressure and cardiac interval using the sequence technique (1). This method has been shown to give similar results to the gold-standard phenylephrine technique (17). Sequences were identified in which systolic blood pressure spontaneously increased or decreased by at least 1 mmHg/beat over at least three consecutive heart beats and, at the same time, cardiac interval changed.

Table 1. Resting values of cardiovascular variables before ingestion of water and saline solution

<table>
<thead>
<tr>
<th></th>
<th>Water</th>
<th>Saline</th>
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<tbody>
<tr>
<td>Systolic blood pressure, mmHg</td>
<td>114 ± 4</td>
<td>113 ± 4</td>
</tr>
<tr>
<td>Mean blood pressure, mmHg</td>
<td>86 ± 3</td>
<td>86 ± 3</td>
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<tr>
<td>Diastolic blood pressure, mmHg</td>
<td>74 ± 3</td>
<td>75 ± 3</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>63 ± 2</td>
<td>63 ± 2</td>
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<tr>
<td>Stroke volume, ml</td>
<td>88 ± 6</td>
<td>87 ± 7</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>5.5 ± 0.3</td>
<td>5.4 ± 0.3</td>
</tr>
<tr>
<td>Total peripheral resistance, mmHg/l min⁻¹</td>
<td>16.2 ± 0.9</td>
<td>16.5 ± 1.1</td>
</tr>
<tr>
<td>Cardiac interval high frequency power, ms²</td>
<td>949 ± 133</td>
<td>1,032 ± 165</td>
</tr>
<tr>
<td>Cardiac interval low frequency power, ms²</td>
<td>1,070 ± 343</td>
<td>1,367 ± 250</td>
</tr>
<tr>
<td>Cardiac interval LF/HF ratio</td>
<td>1.14 ± 0.29</td>
<td>1.39 ± 0.20</td>
</tr>
<tr>
<td>Baroreflex sensitivity, mmHg/mmHg</td>
<td>24.0 ± 2.3</td>
<td>24.6 ± 1.4</td>
</tr>
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Baseline cardiovascular data presented as means ± SE recorded during the 20 min before each of the drinks. LF, low frequency; HF, high frequency.

Fig. 1. Values of systolic (SBP) (A), mean (MBP) (B), and diastolic (DBP) blood pressures (C) before and after water (●) and 0.9% saline (○) drinking. The drinks were ingested between −3 and 0 min. *P < 0.05 compared with baseline.
by at least 4 ms/beat in the same direction. Linear regression was applied to the values of systolic pressure and the subsequent cardiac interval, and the baroreceptor sensitivity was taken as the average regression slope for all sequences with a sufficiently high r² value (≥0.85).

Statistical analysis. All values are reported as mean ± SE. Statistical analysis was performed by ANOVA for repeated measures using statistical software [InStat version 3.01, GraphPad Software (San Diego CA)]. Postdrink values at 10-min time intervals were compared with control values recorded during the 20 min immediately before drinking using Dunnett’s test for multiple comparisons. The areas under the curve of the responses to water and saline drinking were compared by paired t-tests. The level of statistical significance was set at P < 0.05.

RESULTS

Cardiovascular responses to water and saline drinking. Resting values of the cardiovascular variables recorded during the baseline period before ingestion of each of the two drinks are listed in Table 1. The basal hemodynamic state of the subjects was similar for each experimental session. All of the subjects ingested the drinks without problems, and none reported any nausea or other unpleasant effects of the saline drink.

Figure 1 shows the changes in systolic, mean, and diastolic blood pressure after water and saline ingestion. Although both drinks tended to raise blood pressure slightly, the only statistically significant effect was an increase in diastolic blood pressure after the saline drink (P = 0.02).

The time courses of the changes in heart rate, stroke volume, cardiac output and total peripheral resistance are shown in Fig. 2. Heart rate showed a significant and sustained fall after water drinking (P = 0.01) but did not change after the saline drink (P = 0.75). The heart rate responses to the two drinks (areas under the curve) differed significantly (P < 0.01). Both drinks significantly increased cardiac stroke volume (water, P = 0.04; saline, P = 0.02), which reached a peak after 20–30 min and then returned toward baseline. Cardiac output remained stable after the water drink (P = 0.22) but tended to increase slightly after the saline drink (P = 0.13). The areas under the curve for the cardiac output responses to water and saline drinking were significantly different (P = 0.04). Total peripheral resistance increased gradually after water drinking (P < 0.01) but remained unchanged after the saline drink (P = 0.71). The areas under the curve for the total peripheral resistance responses to the two drinks were not quite significantly different (P = 0.11).

Cardiac interval variability and baroreflex sensitivity. Figure 3 shows the changes in cardiac interval high-frequency power and low-frequency/high-frequency (LF/HF) ratio after the water and saline drinks. Water drinking induced an immediate increase in cardiac interval HF power (P = 0.03) that
was sustained for at least 30 min. In contrast, ingestion of the saline drink had no effect on cardiac interval HF power ($P < 0.45$). The area under the curve of the cardiac interval HF power response was significantly higher ($P = 0.02$) after water drinking than after saline drinking. The low-frequency power of cardiac interval variability did not change significantly in response to either the water ($P = 0.10$) or the saline ($P = 0.06$) drinks. There were also no significant changes in the LF/HF ratio of cardiac interval variability after the water ($P = 0.12$) and saline ($P = 0.24$) drinks.

Figure 4 shows the time courses of the changes in cardio-vagal baroreflex sensitivity as calculated using the sequence method. After water drinking, baroreflex sensitivity increased significantly ($P = 0.01$), reaching a peak during the first 30 min before returning toward baseline levels. Saline drinking did not change baroreflex sensitivity ($P = 0.47$).

**DISCUSSION**

The main finding of our study was that saline drinking did not invoke the cardiovascular autonomic responses associated with water drinking. Water drinking elicited a series of cardiovascular changes, including increases in total peripheral resistance, cardiac interval variability and cardio-vagal baroreflex sensitivity, and a decrease in heart rate. These results are consistent with observations from other studies that water drinking activates both the sympathetic (4, 8, 22) and vagal (20) branches of cardiovascular autonomic regulation. That the ingestion of a 0.9% saline solution had no effect on cardiovascular autonomic regulation suggests that the effects of water drinking are influenced by its hypo-osmotic properties.

Water drinking had little effect on blood pressure in our young, healthy subjects, a finding consistent with previous reports (6, 8, 20–22). The slight increase in total peripheral resistance is in line with the observed increase in sympathetic vasomotor discharge after water drinking (22), although the slow time course of the response could also implicate a humoral mechanism. Although water drinking causes a strong vasoconstriction in the forearm and calf (6, 22), we and others (6, 21) have found relatively little or no change in total peripheral resistance. This raises the possibility of concurrent vasodilatation in other vascular beds after water drinking. The fall in heart rate and increases in HF cardiac interval variability and baroreflex sensitivity after water drinking are indicators of an enhanced cardiac vagal tone (18). In young subjects at rest, the cardiac vagal activation after water drinking has been suggested to counteract the effects of the elevated sympathetic tone, resulting in no change in blood pressure (20). Patients whose hearts have been vagally denervated by cardiac transplantation show enhanced pressor responses to water drinking (20).

In contrast to distilled water, drinking an isotonic saline solution did not change heart rate, heart rate variability, baroreflex sensitivity, or total peripheral resistance. These results support the hypothesis that the relative hypo-osmolality of water triggers the cardiovascular responses to drinking. The slight increase in cardiac output after drinking the saline solution was presumably a volume effect mediated by the elevated stroke volume, because heart rate was unchanged.

Fig. 3. Changes in high frequency (HF) cardiac interval variability (power) (A) and low frequency/high frequency (LF/HF) ratio (B) after water (●) and 0.9% saline (○) drinking. The drinks were ingested between −3 and 0 min. *$P < 0.05$ compared with baseline.

Fig. 4. Changes in cardio-vagal baroreflex sensitivity (BRS), as measured by the sequence technique, after water (●) and 0.9% saline (○) drinking. The drinks were ingested between −3 and 0 min. *$P < 0.05$ compared with baseline.
Both drinks caused a similar increase in stoke volume, but the simultaneous fall in heart rate after water drinking ensured that cardiac output did not rise.

Although our results showed that the cardiovascular responses to drinking are influenced by the osmolality of the ingested solution, the site of the osmotic stimulation remains unclear. The responses to water drinking might be mediated by a centrally detected decrease in plasma osmolality. However, sympathetic activity is raised in response to increased, rather than decreased, plasma osmolality (23). Another possibility is that stimulation of osmoreceptive nerve fibers that are thought to exist in the gut or portal circulation (9, 16, 26) might play a role. The osmotic effects of water drinking in these regions are probably greater than the reported 2–3% decrease (2) in venous plasma osmolality. Therefore, local stimulation of osmoreceptors after water drinking could potentially invoke responses, even without any major changes in overall plasma osmolality.

We also considered that factors other than osmotic stimulation could account for the contrasting cardiovascular autonomic responses to water and saline drinking. For example, the different tastes of the drinks might influence the initial responses, but this is unlikely to account for the sustained effects. The two drinks might also be emptied from the stomach at different rates, although studies have shown that osmolality has little or no effect on gastric emptying (15, 24, 28). Another possibility is that water and saline drinking might have differing effects on the levels of vasoactive hormones such as vasopressin or ANG-II. We did not measure hormonal concentrations, as we wanted to avoid influencing the autonomic responses by taking blood samples. Jordan et al. (8) found no measurable changes in vasopressin or plasma renin activity at 30 and 60 min after drinking half a liter of water, although this does not rule out transient changes occurring earlier. Furthermore, in dehydrated humans, drinking water or isotonic saline results in a similar fall in vasopressin concentrations and no change in plasma renin activity (5). It is therefore unlikely that vasopressin accounts for the contrasting cardiovascular effects of water and saline ingestion.

In patients with autonomic failure, water ingestion can cause a marked and potentially dangerous rise in blood pressure of 30 mmHg or more. Interestingly, the pressor effect of water occurs in these patients despite them showing severely impaired responses to standard tests of sympathetic function (8). This intriguing finding has led to the suggestion that nonautonomic factors, such as hyperosmolarity to changes in fluid balance, may be responsible for the pressor response to water drinking (4, 14). In our study, drinking isotonic saline, which would be expected to induce a greater plasma volume increase than water (5), failed to elicit the cardiovascular responses associated with drinking water. Our results therefore support the concept that, rather than being a volume effect, the cardiovascular responses to water in healthy subjects can be attributed to reflexes mediated by its hyposmolality.

The autonomic response to water drinking is rather unusual, consisting of simultaneous sympathetic and vagal activation. This would explain the lack of change in LF/HF ratio, which is considered to reflect sympathetic balance (12). Such a response is not unique in physiology because facial cooling also invokes a reflex that involves cardiovascular activation, bradycardia, and peripheral vasoconstriction, which might be useful in enhancing survival during immersion in cold water (the “diving reflex”) (3). However, in contrast to the diving reflex, the cardiovascular responses to water (but not saline) drinking do not seem to have an obvious biological purpose.

We conclude that osmolality contributes to the sympathetic and parasympathetic activation observed in healthy subjects after water drinking. These results are consistent with the existence of osmoreceptive nerve fibers in the gut or portal circulation that can influence cardiovascular autonomic regulation in humans. The osmotically induced increase in cardiovascular tone after water drinking probably contributes to buffering the vasoconstrictor response in young healthy subjects.

REFERENCES


