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Thirst response to acute hypovolaemia in healthy women and women prone to vasovagal syncope

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HIGHLIGHTS

- Self-perceived thirst score increased three-fold when LBNP of 40 mm Hg was applied.
- Thirst increase in women prone to vasovagal syncope was doubled compared to controls.
- Plasma concentrations of angiotensin II increased in response to hypovolaemia, but did not correlate to thirst.
- Angiotensin II increase was positively correlated to hypovolaemia-induced increased heart rate.

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ABSTRACT

The present study measured self-perceived thirst and plasma angiotensin II (ATII) concentrations during graded hypovolaemic stress, induced by lower body negative pressure (LBNP), to elucidate the dependence of thirst on haemodynamics. A total of 24 women aged between 20 and 36 (mean age, 23) years rated their thirst on a visual analogue scale, graded from 0 to 100, when LBNP of 20, 30 and 40 mm Hg was applied. Half of the women had a history of vasovagal syncope (VVS). The results showed that the thirst score increased three-fold when LBNP was applied, from 11 (median; 25th–75th percentiles, 9–25) to 34 (27–53; $P < 0.001$). The women in the VVS group had twice as great an increase as those without a history of VVS ($P < 0.02$). The plasma ATII concentration increased significantly in response to LBNP, both in the VVS group and in the control group, but the changes did not correlate with thirst. Application of LBNP decreased systolic and mean arterial pressures, cardiac output and pulse pressure ($P < 0.001$ for all), but thirst correlated only with increase in heart rate and, independently, with reduction of mean arterial pressure. In conclusion, thirst and ATII increase in response to hypovolaemic stress, but are not statistically related. The haemodynamic parameter that was most strongly related to thirst was tachycardia.

1. Introduction

Thirst is a sensation that is aroused by a need for water, which is crucial for maintaining homeostasis of the body fluids [1,2]. High osmolality is a known signal for thirst, and additional factors include hypovolaemia and release of angiotensin II (ATII). Knowledge of the aetiology of thirst is important for our understanding of how body fluid homeostasis is maintained and also enables us to treat the excessive thirst that is a feature of certain disease states, such as heart failure [3–5]. The current view of the relationship between ATII and thirst is primarily based on animal studies [1,6,7], while human thirst trials reveal a less clear picture [8]. Previous findings about the role of AT II on the regulation of thirst are difficult to generalize for thirst in humans [7,9,10].

One situation in which increased thirst occurs is hypovolaemia, in which blood volume is reduced, due to events such as bleeding, pooling or dehydration. Hypovolaemia has profound effects on venous filling, venous return, and cardiac output [11,12] and the responses may reveal different characteristics in individuals suffering from vasovagal syncope (VVS) attacks [13]. Lower body negative pressure (LBNP) is an excellent model for hypovolaemic circulatory stress, as it induces central hypovolaemia and unloading of

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baroreceptors with activation of the sympathetic autonomic system [12]. Orthostatic tolerance to LBNP is decreased in individuals with induced hypovolaemia as well as in young women [14,29]. Low blood volume might also play a role in the pathophysiology of VVS [15]. The ATII response to LBNP has not been studied in patients suffering from VVS.

We therefore chose to study the sensation of thirst during hypovolaemia in women suffering from recurrent VVS as well as in women without a history of syncope. Our aim was to examine whether thirst increases during acute hypovolaemic stress and whether ATII, haemodynamic parameters or a history of VVS can be statistically related to any inferred change.

2. Materials and methods

2.1. Volunteers

A total of 24 women, age between 20 and 36 (mean age 23) years volunteered and participated in the study. Their mean (SD) body height was 165 (6) cm, mean body weight was 63 (11) kg and mean BMI was 23.0 (3.5) kg/m^2. Three additional volunteers were excluded, due to missing data (n = 1) or to both objective and subjective signs of presyncope during the protocol (n = 2). The participants had declared themselves to be non-smokers and free from cardiopulmonary disease, and were not taking medications that affect the cardiovascular system.

The volunteers were selected from two different cohorts; those who had a history of VVS (VVS group) and those who had never experienced syncope (control group). Eleven volunteers had previously been investigated due to clinically relevant syncope in daily life, and had all been diagnosed with VVS during a positive tilt table test. Moreover, they all had a negative cardiovascular examination and were found otherwise healthy, ruling out cardiac syncope. The women with VVS were recruited from a database in the Department of Clinical Physiology in Linköping. The healthy controls were recruited from the general population; they had never experienced syncope and were matched regarding age and fitness level.

All women were scheduled in the follicular phase (days 2–10) of the menstrual cycle. Five women in the VVS group, but none in the control group, were on oral contraceptives; similar studies conducted in our laboratory have not detected any significant impact of oral contraceptive use on cardiovascular findings [16]. All volunteers gave written, informed consent to the experiments, which were approved by the regional ethical review board in Linköping, in accordance with the Declaration of Helsinki.

2.2. Procedure

The participants arrived at the Department of Clinical Physiology at random, either in the morning or the afternoon, having had a light meal 1 h prior to arrival. They had been instructed to abstain from vigorous-intensity activity and beverages containing caffeine for the 24 h preceding the experiments. To ensure optimal fluid balance typical for each volunteer, they were all instructed to drink 1 L of water on the evening prior to the experiments, allowing the night time for excretion of excess fluid.

The participants were not permitted to drink for 45 min prior to, as well as during, the experiments, which were performed at a stable room temperature of 25 °C. The study began after the participants had rested in the supine position for 30 min to reach haemodynamic steady-state. Immediately after the participant was placed in the supine position, an indwelling catheter was inserted in the left antecubital vein.

2.2.1. Lower body negative pressure

In the supine position, the lower part of the body up to the level of the iliac crest, was enclosed in an airtight box with a seal fitted hermetically around the waist [11]. The box was connected to a vacuum source that permitted a stable negative pressure to be produced within 5 s and to be continuously measured with a rheostat. Experiments were performed at LBNP of 0, 20, 30 and 40 mm Hg, which were maintained for 4–5 min each. To assure return to the basal state in blood pooled to the lower part of the body, blood pressure and peripheral resistance, a break of 3–4 min between each LBNP step was permitted.

2.3. Measurements

The measurements included assessment of thirst, blood sampling of ATII and central haemodynamics at baseline and after application of LBNP. Heart rate variability (HRV) was analysed from electrocardiogram (SphygmoCor®, AtCor Medical Pty Ltd, West Ryde, Australia) recordings of heart rate.

2.3.1. Thirst

Perceived thirst intensity was assessed using a visual analogue scale (VAS), which has previously been used to evaluate thirst in patients with cancer, renal failure and heart failure, as well as during trauma resuscitation [3–5,10]. The volunteers were informed just before the experiments started that they would be asked to rate their thirst sensation. They did not receive any information prior to or during the experiments about thirst or that thirst intensity might change.

The participants were asked to grade their thirst from 'none' (0 mm) to 'worst possible' (100 mm), by marking a cross at the appropriate point on a 100 mm line. The volunteers were in the supine position in the LBNP chamber and strapped down with equipment, which meant that they were unable to move their arms. Therefore, the researcher moved a pencil along the line and the volunteers stated where on the line they wanted the cross to be placed. The researcher who performed the thirst assessments during the experiments had no preconceived stance on thirst or on the impact of LBNP on thirst.

2.3.2. Angiotensin II

A venous blood sample for measurement of ATII was withdrawn from each participant, at baseline and at the end of each 4-min period of LBNP, in a cold anticoagulated tube. These samples were immediately placed in an ice bath and cold centrifuged within 20 min of being taken. The plasma samples were then stored at −70°C until analysed (Study Centre, Clinical Chemistry, Karolinska University Laboratory, Stockholm, Sweden). The plasma concentration of ATII was measured with a radio-immunological method after separation with Sep-Pak C-18 and incubation for approximately 24 h with antibodies from rabbit directed against ATII. A trace amount of ^{125}I-ATII was then added, and the incubation continued for an additional 6 h. The bound and free ATII were then separated using a second antibody directed against the rabbit antibodies. After centrifugation and decanting, the ^{125}I activity was taken as the measure of the plasma concentration of ATII. The coefficient of variation was 8.6% in the studied range.

2.3.3. Haemodynamics

Heart rate and arterial pressure were monitored non-invasively, beat-by-beat (Finometer® Midi, Finapres Medical Systems, Amsterdam, the Netherlands). A Vivid E-9 ultrasound scanner (GE Healthcare, Wauwatosa, WI, USA) with a transthoracic 4 MHz probe and a non-imaging 2.5 MHz Doppler probe was used to measure stroke volume. Prior to arrival at the laboratory, the participants had a routine echo to rule out structural cardiac disease and to measure left ventricular (LV) size, ejection fraction, cardiac output and stroke volume, based on the volume measurement according to Teichholz formula (Table 1). During the experiments, each participant was in the supine position flat on her back, and it was not always possible to obtain acceptable Doppler