Cardiovascular Drift is Related to Reduced Maximal Oxygen Uptake During Heat Stress

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Running Head: Cardiovascular drift and $\dot{V}O_{2max}$

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ABSTRACT

Introduction/Purpose: This study investigated whether the progressive rise in heart rate (HR) and fall in stroke volume (SV) during prolonged, constant-rate, moderate-intensity exercise (cardiovascular drift, CVdrift) in a hot environment is associated with a reduction in $\dot{V}O_{2max}$. **Methods:** CVdrift was measured in nine male cyclists between 15 and 45 min of cycling at 60% $\dot{V}O_{2max}$ in 35°C that was immediately followed by measurement of $\dot{V}O_{2max}$. $\dot{V}O_{2max}$ also was measured after 15 min of cycling on a separate day, so that any change in $\dot{V}O_{2max}$ between 15 and 45 min could be associated with the CVdrift that occurred during that time interval. This protocol was performed under one condition in which fluid was ingested and there was no significant body weight change (0.3±0.4%) and under another in which no fluid was ingested and dehydration occurred (2.5±1%, p<0.05). **Results:** Fluid ingestion did not affect CVdrift or change in $\dot{V}O_{2max}$. A 12% increase in HR (151±9 vs. 169±10 beats·min^{-1}, p<0.05) and 16% decrease in SV (120±12 vs. 101±10 mL·beat^{-1}, p<0.05) between 15 and 45 min was accompanied by a 19% decrease in $\dot{V}O_{2max}$ (4.4±0.6 vs. 3.6±0.4 L·min^{-1}, p<0.05) despite attainment of a higher maximal HR (p<0.05) at 45 min (194±5 bpm) vs. 15 min (191±5 bpm). Submaximal $\dot{V}O_2$ increased only slightly over time, but %$\dot{V}O_{2max}$ increased from 63±5% at 15 min to 78±8% at 45 min (p<0.05). **Conclusion:** We conclude CVdrift during 45 min of exercise in the heat is associated with decreased $\dot{V}O_{2max}$ and increased relative metabolic intensity. The results support the validity of using changes in HR to reflect changes in relative metabolic intensity during prolonged exercise in a hot environment in which CVdrift occurs.

Keywords: circulation, heart rate, oxygen consumption, stroke volume, thermoregulation

Paragraph Number 1 After about 10 minutes of prolonged, constant-rate, moderate-intensity (50-75% of maximal oxygen uptake, $\dot{V}O_{2max}$) exercise, a slow, progressive change over time, or drift, occurs in several cardiovascular measures. Heart rate (HR) increases progressively; stroke volume (SV), mean arterial and pulmonary pressures decrease progressively; while cardiac output ($\dot{Q}$) remains relatively constant (11,25). Cardiovascular drift (CVdrift) drift is observed in thermoneutral (11) and warm (20) environments, but greater changes occur in a warm environment (13).

Paragraph Number 2 The mechanism underlying CVdrift is controversial (6). One hypothesis is that CVdrift is caused by peripheral displacement of the blood volume with progressive increases in cutaneous blood flow and venous volume causing the progressive fall in central venous pressure, SV and arterial pressure (11,16,25). An alternate hypothesis is that the progressive increase in HR caused by hyperthermia and increased sympathetic nervous system activity decreases ventricular filling time, end-diastolic volume and SV (6).

Paragraph Number 3 Regardless of the cause, the consequence of CVdrift for physical work capacity is not fully understood. Studies that have measured $\dot{V}O_{2max}$ following prolonged exercise suggest that under thermoneutral conditions, CVdrift is associated with a modest (5 – 12%) reduction in $\dot{V}O_{2max}$ (10,29,30). However, in these studies, $\dot{V}O_{2max}$ was not measured at the same points in time as the variables characterizing CVdrift. Thus, it is uncertain whether the altered $\dot{V}O_{2max}$ accurately reflected the effect of CVdrift. Furthermore, the effect on $\dot{V}O_{2max}$ of CVdrift that occurs during prolonged exercise in a hot environment is unresolved (13).

Paragraph Number 4 Whether CVdrift is associated with a reduction in $\dot{V}O_{2max}$ or not is an important issue, with practical implications for the use of HR for prescription of exercise intensity. Intensity of exercise is commonly prescribed

using HR, based on the strong relation between percent of maximal HR or percent of HR reserve (%HRR), and relative metabolic intensity as reflected by %$\dot{V}O_{2max}$ or percent of oxygen uptake reserve (%$\dot{V}O_2R$) (1). However, the use of HR as an indicator of relative metabolic intensity is based on validation studies that employed short-term exercise of progressively increasing intensity (8,35). Whether change in HR is a valid indicator of change in relative metabolic intensity during more prolonged exercise is uncertain.

Paragraph Number 5 The primary purpose of our study was to determine whether CVdrift was associated with a reduction in $\dot{V}O_{2max}$ during prolonged exercise in a hot environment. This was accomplished by measuring CVdrift between 15 and 45 min of cycling and then immediately measuring $\dot{V}O_{2max}$. $\dot{V}O_{2max}$ also was measured immediately after 15 min of cycling on a separate day so that any change in $\dot{V}O_{2max}$ between 15 and 45 min could be associated with the CVdrift that occurred in the same time interval. Forty-five min of exercise was selected because this is a duration during which considerable CVdrift occurs (11) and which is typical of aerobic exercise used for conditioning. To determine the extent to which any relation of CVdrift to $\dot{V}O_{2max}$ was accounted for by dehydration, the protocol above was completed under one condition in which no fluid was ingested (NF) and during a second condition in which fluid was ingested to prevent dehydration (F). Because studies on the effect of fluid ingestion on the magnitude of CVdrift when the duration of exercise is less than 1 hr have been equivocal (20,22), we were uncertain whether any effect would be evident. We hypothesized that the increase in HR and decrease in SV between 15 and 45 min of submaximal exercise would be associated with reduced $\dot{V}O_{2max}$ and increased relative metabolic intensity, and that fluid ingestion would reduce the magnitude of CVdrift and reduction in $\dot{V}O_{2max}$.

METHODS

Subjects

Paragraph Number 6 Nine healthy men volunteered as subjects. This sample size is sufficient to detect a five percent decrease in $\dot{V}O_{2max}$ using a two-tailed t test for dependent samples at $\alpha = 0.05$ and statistical power of 0.8, assuming individuals have a mean $\dot{V}O_{2max}$ of 55 mL·kg^{-1}·min^{-1} with a SD of 7 mL·kg^{-1}·min^{-1} and that the test-retest correlation for $\dot{V}O_{2max}$ is 0.95 (18). Subject physical characteristics (means $\pm$ SD) were: age $= 25 \pm 4$ yr, mass $= 71.8 \pm 5.1$ kg, height $= 179.0 \pm 5.0$ cm, and percent body fat [using the Jackson-Pollock equations for predicting body density from seven skinfolds in men (15) and the Siri equation to determine percent fat from body density (34)] $= 8.1 \pm 3.7\%$. The subjects were trained cyclists averaging 116 ± 98 km·week^{-1} and runners averaging 34 ± 19 km·week^{-1}, or subjects who trained cycling and running for a combined 6 h·week^{-1} during the previous 6 mo. The study was approved by the University's Institutional Review Board, and written informed consent was obtained prior to testing.

Research Design

Paragraph Number 7 A repeated measures experimental design was used in which subjects were tested under all conditions. Following acclimation rides and a control $\dot{V}O_{2max}$ test, four experimental trials in which subjects cycled for either 15 or 45 minutes at 60% $\dot{V}O_{2max}$ were completed on separate days. Subjects completed two trials with no fluid ingestion (15NF and 45NF) and two trials with fluid ingestion (15F and 45F), followed immediately by measurement of $\dot{V}O_{2max}$. For the fluid trials, equal volumes of tap water at 35°C were ingested just prior to beginning exercise and at 10 min (15F), or just prior to beginning exercise and at 10 min, 25 min, and 35 min (45F), respectively. The volume of water ingested was designed to prevent dehydration and was based on the sweat rate measured during the last acclimation ride plus the estimated additional sweat loss that would occur during

the $\dot{V}O_{2max}$ test portion of the protocol. The order of conditions and trials within each condition was randomized, but the two trials for each condition were performed in succession. All trials occurred in an environmental chamber at 35°C, 40% relative humidity (RH) without fan airflow. Each subject was tested at the same time of day to minimize the effects of circadian variation in HR and core temperature, and trials were separated by one day.

Protocol and Procedures

Paragraph Number 8 Acclimation. Prior to testing, subjects completed a 4-d protocol designed to acclimate them to the environmental conditions under which the experimental trials were performed and to provide practice with procedures. The protocol consisted of cycling 1 h per day at 60% HRR in an environmental chamber at 35°C, 40% RH without fan airflow. Rides occurred on successive days and at the same time each day. Nude body weight was measured to the nearest 10 g with an electronic scale (A&D Co., Ltd., Tokyo, model FW-150KA1) before and after each ride for determination of sweat rate. During the last two trials, the CO_2-rebreathing procedure for measuring cardiac output was practiced.

Paragraph Number 9 Control $\dot{V}O_{2max}$. Two days after the fourth acclimation ride, subjects completed a control graded exercise test (GXT) to measure $\dot{V}O_{2max}$. Subjects reported to the laboratory following a 3-h fast, but they were well hydrated. They were instructed not to consume alcohol, caffeine, or non-prescription drugs the day before and the day of testing. On the morning of the test, subjects completed a 24-h history questionnaire designed to determine adherence to pretest instructions. Testing was conducted on an electronically-braked cycle ergometer (Lode Excalibur Sport, Lode B.V., Groningen, NL) in an environmental chamber maintained at 22°C, 40% RH. Following a warm-up, the GXT began with subjects cycling at 200 W, with power

output increased 25 W every 2 min until subjects could no longer continue pedaling. $\dot{V}O_2$ and related gas exchange measures were determined by indirect calorimetry over 30-s intervals using a Parvo Medics TrueOne 2400 Metabolic Measurement System (Parvo Medics, Inc., Salt Lake City, UT). HR and ratings of perceived exertion (RPE) were measured each minute. HR was measured with a Polar® Vantage XL heart rate monitor (Polar Electro, Inc. Woodbury, NY, model 145900). RPE was measured by the Borg 6-20 scale using standardized instructions (4). Three minutes after completion of the test, a finger-stick blood sample was obtained for determination of blood lactate. Blood lactate concentration was measured using a YSI 2300 Stat Plus Analyzer (Yellow Springs Instruments, Inc., Yellow Springs, OH).

Paragraph Number 10 To ensure that a plateau in $\dot{V}O_2$ was attained, subjects completed an additional bout of cycling following 20 min of rest. Subjects cycled to exhaustion at a power output equivalent to the last workload performed during the graded test (if < 1 min was completed during the last stage of the graded test) or at a power output 25 W higher than the last workload performed during the graded test (if ≥ 1 min was completed during the last stage of the graded test).

Paragraph Number 11 Attainment of $\dot{V}O_{2max}$ (average of the two highest consecutive 30-s values) was determined by attainment of a plateau as evidenced by an increase in $\dot{V}O_2$ between the last two stages of < 135 mL·min^{-1}, which is half the expected increase in $\dot{V}O_2$ of 270 mL·min^{-1} based on the American College of Sports Medicine metabolic equation (1):

$$\dot{V}O_2 = (10.8 \bullet W \bullet M^{-1}) + 7,$$

where $\dot{V}O_2$ is gross oxygen consumption in mL·kg^{-1}·min^{-1}, W is power in watts, and M is body mass in kg. Using this protocol, all subjects demonstrated a plateau in $\dot{V}O_{2max}$, either during the GXT (3 subjects) or during the subsequent bout (6 subjects).

Paragraph Number 12 *Experimental trials.* Subjects arrived at the laboratory after following the same pre-test instructions provided for the control GXT. Adherence to instructions was verified using the 24-h history questionnaire. Tympanic temperature (T_t) and urine specific gravity (USG) were measured to verify subjects did not have a fever ($T_t < 37.8°C$) and were adequately hydrated (USG < 1.030). Subjects then measured their nude body weight and inserted a rectal temperature probe. Next, a Teflon® venous catheter was inserted into an antecubital vein and was kept patent with 0.5 mL of 10 USP units·mL^{-1} heparin lock flush. Subjects then sat upright for 20 min in order for plasma volume to stabilize while skin temperature probes were attached, resting HR was measured, and blood samples were drawn. Subjects then began cycling on the Lode ergometer at a power output estimated to elicit 60% $\dot{V}O_{2max}$. In 45F and 45NF, metabolic, cardiovascular and perceptual measures were taken between min 8 and min 15 and between min 38 and 45. Systolic (SBP) and fourth-phase diastolic (DBP) blood pressures were measured by ascultation, RPE was obtained, blood samples were drawn, expired air was analyzed for 2 min for measurement of $\dot{V}O_2$ and $\dot{V}CO_2$ using the Parvo Medics system, HR was measured using the Polar® HR monitor, and two trials of CO_2-rebreathing were performed for measurement of $\dot{Q}$, in that order.

Paragraph Number 13 At the end of either 15 or 45 min of cycling during all four experimental trials, subjects immediately began a GXT with no cessation of cycling. Power output was initially increased 25 W above the power output maintained during the submaximal exercise (60% $\dot{V}O_{2max}$), with additional 25-W increases in power output every 2 min until the subject could not continue. $\dot{V}O_2$ and other metabolic measures were measured over 30-s intervals, HR was measured each min, and RPE was obtained every 2 min and at the point of exhaustion. Blood samples were drawn 3 min following the termination of the test and nude body weight was re-measured. The measure of $\dot{V}O_{2max}$ on the experimental trials was

considered valid if 1) the plateauing criterion used for the control test was met (4 subjects for 45F, 4 for 15 NF and 3 for 45 NF) or 2) if a HR within 5 bpm of that on the control test was obtained (remainder of tests).

Paragraph Number 14 $\dot{Q}$ was measured using the indirect-Fick CO_2-rebreathing method, as described by Jones (17), using the Parvo Medics metabolic system and software. This involved measuring the $\dot{V}CO_2$, end-tidal CO_2 concentration, and the equilibrium CO_2 concentration following rebreathing in succession. Two rebreathing trials, separated by approximately one min, were always performed and averaged. The reliability of values from the two trials was high (intraclass correlation = 0.93). SV was calculated by dividing cardiac output by HR. Mean arterial pressure (MAP) was estimated as MAP = DBP+0.33(SBP-DBP). Systemic vascular resistance (SVR) was calculated by dividing MAP by $\dot{Q}$.

Paragraph Number 15 Rectal temperature (T_{re}) was measured using a temperature probe (Ellab, Inc., Arvada, CO, model MOV-55044-A) inserted 10 cm past the anal sphincter. Skin temperature was measured using temperature probes (Ellab, Inc., Arvada, CO, model MHF-18058-A) attached on the back, forearm and thigh. Rectal and skin temperature probes were connected to a temperature data acquisition system (Ellab, Inc., model TM9608 with Eval 2.1 software), which collects and stores temperatures continuously. Mean skin temperature (T_{sk}) was calculated according to the formula of Burton (5):

$$T_{sk} = 0.5 \cdot T_1 + 0.36 \cdot T_2 + 0.14 \cdot T_3,$$

where T_1, T_2, and T_3 are back, thigh, and forearm skin temperatures, respectively. Mean body temperature ($\overline{\overline{T}}_b$) was calculated from T_{re} and T_{sk} with the formula of Baum et al. (3):

$$T_b = 0.87 \cdot T_{re} + 0.13 \cdot T_{sk}.$$

Paragraph Number 16 Blood samples were drawn into 2- and 4-mL vacutainers containing EDTA. Samples used for catecholamine analysis (4 mL) were immediately refrigerated, centrifuged at 4°C within 1 h and the plasma stored at -80°C until analyzed. The other samples (2 mL) were used to measure hemoglobin in duplicate with a HemoCue B-Hemoglobin photometer and hematocrit in triplicate with the microhematocrit method. Plasma volume (PV) change during cycling relative to pre-exercise rest was estimated from measures of hemoglobin and hematocrit using the Dill-Costill equation (9).

Paragraph Number 17 Plasma norepinephrine (NE) and epinephrine (E) were quantified by high performance liquid chromatography with electrochemical detection after alumina extraction of 250 µL plasma. A refrigerated autosampler (Waters 717-plus, Milford, MA) and a pump (Waters 510, Milford, MA) were used in conjunction with a glassy carbon working electrode set at +650 mV and a range of 0.5 nA with respect to an Ag/AgCl pulsed electrochemical detector (Waters 464 pulsed Electrochemical Detector, Milford, MA). A C12, 4 µm, reverse-phase column (Phenomenex Synergi, 4 µ, Max-RP, 150. 0 × 4. 6 mm) was used. Chromatograms were monitored, recorded, and analyzed with Millennium 32 software (Version 3, 1999; Millipore, Milford, MA). Peaks were quantified by height and compared with daily standard lines fitted by regression analysis to a series of 4-5 standards that were analyzed throughout the day. Correlation coefficients for these daily standard lines always exceeded 0.98. The detection limit of the assay was 1 pg per sample. Standards (Sigma Chemical, St. Louis, MO) were solubilized in mobile phase and stored at -70ºC until used (approximately 2 weeks after preparation). The mobile phase was a 0.1 M phosphate buffer with 0.1 M EDTA, 0.25 M octanesulfonic acid, and 4.5% acetonitrile in ultrapure water (18 megohms·cm^{-1} resistance; pH 3.10). The mobile phase was filtered through a C18

cartridge (Alltech, Deerfield, IL), degassed by helium sparging, and delivered at a flow rate of 1.0 mL·min^{-1}.

Paragraph Number 18 To evaluate the comparability of changes in HR during submaximal exercise and changes in relative metabolic intensity caused by possible changes in $\dot{V}O_2$ during submaximal exercise or $\dot{V}O_{2max}$, %HRR and   %$\dot{V}$ O$_2$R utilized during submaximal exercise were calculated. %HRR was calculated as: [(HR$_{ex}$- HR$_{rest}$)/(HR$_{max}$ - HR$_{rest}$)] × 100. %$\dot{V}O_2$R was calculated as: [($\dot{V}O_{2ex}$ - 3.5)/($\dot{V}O_{2max}$ - 3.5)] × 100. Resting HR was measured using the Polar$^{®}$ HR monitor in the environmental chamber with the subject upright on the cycle ergometer prior to beginning the submaximal exercise.

Statistical Analysis

Paragraph Number 19 Statistical analyses were performed using SPSS v. 11 for Windows (SPSS, Inc., Chicago, IL). Data are reported as means ± SD unless specified otherwise. A 2 × 2 (Condition × Time) ANOVA with repeated measures on both factors was used to test the significance of mean differences between fluid conditions and between 15 and 45 min in time, and their interaction. Repeated t tests were used to test for simple effects. A one-way ANOVA with repeated measures, with follow-up repeated-measures t-tests and the Bonferroni α correction was used to compare means from the four experimental tests and the control $\dot{V}O_{2max}$ test. An α level of 0.05 was used for all significance tests.

RESULTS

Paragraph Number 20 *Hydration status and fluid ingestion.* There was no difference (p > 0.05) in mean body mass (71.8 ± 5.1 – 72.2 ± 4.8 kg) or urine specific gravity (1.007 ± 0.006 – 1.012 ± 0.007) prior to the control or experimental exercise tests, suggesting hydration status was similar at the beginning of all tests. Fluid ingested during 15F (700 ± 103 mL) and 45F (1778 ± 249 mL) was successful in preventing dehydration during the bouts of submaximal exercise and the

subsequent GXT to measure $\dot{V}O_{2max}$. The body mass percent change from rest in

15F and 45F were each -0.3%, which was smaller (p < 0.05) than the body mass

percent change from rest in 15NF (-1.4%) and 45NF (-2.5%). Despite this

difference in percent change in body mass between fluid and no fluid conditions,

two-way ANOVAs indicated that fluid ingestion did not significantly affect

CVdrift (Δ SV or Δ HR), change in $\dot{V}O_{2max}$ from control, or other measures that

affected the tests of our hypotheses. Therefore, data from the two conditions were

combined to simplify presentation.

   Paragraph Number 21 *Responses to submaximal exercise*. Changes in

responses between min 15 and min 45 of submaximal exercise are contained in

Table 1 and Figure 1. $\dot{V}O_2$ and blood lactate concentration increased only slightly

(p < 0.05) over time, with the relative metabolic intensity averaging 63% of the

control $\dot{V}O_{2max}$ and blood lactate concentration ~2.5 mmol·L^{-1}. A substantial

CVdrift occurred as evidenced by an 18 beat·min^{-1} (12%) increase in HR (p < 0.05)

and a 19 mL (16%) decrease in SV (p < 0.05) (Figure 1). $\dot{Q}$ decreased (p < 0.05) by

1 L·min^{-1} (6%) and O_2 pulse decreased (p < 0.05) by 10%. MAP was unchanged,

but SVR increased (p < 0.05) by about 5%. PV change from rest increased (p <

0.05) about 2 percentage points. NE increased (p < 0.05) 64% but E did not change

significantly (9.8%, p > 0.05). T_{re}, T_{sk} and T_b increased (p < 0.05) by 1.0, 0.3, and

1.0°C, respectively. RPE increased (p < 0.05) by about 2 points.

   Paragraph Number 22 *Responses to maximal exercise*. Data on $\dot{V}O_{2max}$

and related measures from the control and experimental tests are presented in Table

2. $\dot{V}O_{2max}$, HR_{max}, O_2 pulse and RPE measured after 15 min of submaximal

exercise were not different (p > 0.05) from the control test, although these values

were achieved at lower power output and in less time as well as being accompanied

by lower (p < 0.05) levels of $\dot{V}_E$, RER and blood lactate. $\dot{V}O_{2max}$ measured after 45

min of submaximal exercise was decreased (p < 0.05) by 19% compared to the tests

following 15 min of submaximal exercise. A similar pattern was observed for maximal power output, test duration, $\dot{V}_E$, O_2 pulse, blood lactate and NE. There were no differences in maximal RER, ΔPV, RPE, and T_{sk} between the tests following 15 and 45 minutes of submaximal exercise. Maximum HR following 45 min of submaximal exercise was higher than control (p < 0.05) and values measured following 15 min of submaximal exercise (p < 0.05), by 3-4 beats·min^{-1}. T_{re} and T_b also were higher by ~1.0°C, and E was higher by 37%.

Paragraph Number 23 *Measures of exercise intensity.* Data on measures of exercise intensity based on the $\dot{V}O_{2max}$ values obtained during the control graded exercise test (GXT) and at the respective time points are provided in Table 3. Because $\dot{V}O_{2max}$ was reduced after 45 min of submaximal exercise, %$\dot{V}O_{2max}$ increased accordingly. Likewise, the drift in HR resulted in a higher %HR_{max} at 45 min compared with 15 min. The change in %$\dot{V}O_2R$ over time (16.5 ± 9.1) was greater than the change in %HRR (13.0 ± 5.2) over time, but 45-min values were similar. Figure 2 shows that the individual changes in %HRR and %$\dot{V}O_2R$ were significantly related. The regression coefficient indicated each 1 unit increase in %HRR was accompanied by a 1.24 unit increase in %$\dot{V}O_2R$.

DISCUSSION

Paragraph Number 24 Cardiovascular drift is a well established phenomenon (6,25). However, it is not clear whether the progressive increase in HR and decrease in SV over time are benign with little implication for performance, or whether they reflect altered $\dot{V}O_{2max}$ and thus have implications for performance and exercise prescription. Our primary purpose was to determine whether or not CVdrift is associated with a change in $\dot{V}O_{2max}$, and to determine the implications for prescription of exercise intensity for people exercising to develop aerobic fitness. A limitation of the study was that subjects were a homogeneous population of young, fit males who were tested under specific environmental conditions. Thus,

applying the current findings to a population and/or environment different from the one employed in this study warrants caution.

Paragraph Number 25 The main finding of this study is that CVdrift, as reflected by the fall in SV and rise in HR over time, is accompanied by a decrease in $\dot{V}O_{2max}$ during 45 min of submaximal, constant-rate exercise in a hot environment. Because submaximal $\dot{V}O_2$ increased only slightly, the decrease in $\dot{V}O_{2max}$ increased the relative metabolic intensity during submaximal cycling. The data provide support for the validity of using changes in HR to reflect changes in relative metabolic intensity during prolonged exercise in a hot environment in which CVdrift occurs.

Paragraph Number 26 We designed a protocol that previous studies (11,21,33) have shown should cause considerable CVdrift using an intensity and duration of exercise typically utilized for conditioning. In accordance with our expectation, considerable CVdrift occurred; HR increased 18 beats$\cdot$min^{-1} (12%) and SV decreased 19 mL (16%) between 15 and 45 min of exercise. In comparison to other studies measuring CVdrift under similar ambient temperatures, the magnitude of CVdrift that occurred was greater in the current study; however, these studies employed the use of a fan (19,20), which would presumably lower the amount of thermal strain and accompanying CVdrift. A study by Fritzsche et al. (12) utilized a lower ambient temperature (27°C), but changes in HR (11% increase) and SV (13% decrease) were similar to those of the current study.

Paragraph Number 27 Because studies on the effect of fluid ingestion on the magnitude of CVdrift when the duration of exercise is less than 1 hr have been equivocal (20,22), we wanted to determine whether or not dehydration might account for any change in CVdrift under the conditions of our study. Dehydration by 2.5% during the 45 min of submaximal exercise combined with the subsequent $\dot{V}O_{2max}$ test in NF had no effect on the primary measures of CVdrift, namely HR and

SV, or on the change in $\dot{V}O_{2max}$ between 15 and 45 min, compared to the condition in which dehydration was prevented. The lack of a differential effect on $\dot{V}O_{2max}$ is not surprising in light of the work of Nybo et al. (23). In that study, investigators determined that marked skin and core body hyperthermia alone or combined with dehydration by 4% was associated with a 16% reduction in $\dot{V}O_{2max}$. Since T_{re} was similar between F and NF conditions in the present study, $\dot{V}O_{2max}$ was equally affected. Furthermore, Montain et al. (20) demonstrated under similar conditions but with fan cooling that differences in T_{re} between F and NF conditions did not manifest until 80 min into exercise. Thus, despite no fan cooling (which would presumably cause differences in T_{re} between fluid conditions to manifest sooner) in the current study, it is possible that the 45 min duration of exercise was insufficient to elicit the consequences of dehydration necessary to differentially influence the magnitude of CVdrift or reduction in $\dot{V}O_{2max}$.

Paragraph Number 28 As mentioned, the lack of an effect of dehydration on $\dot{V}O_{2max}$ is not surprising based on the findings of Nybo et al. (23). However, these findings were contrary to that of Craig and Cummings (7), who found that dehydration by 1.9% and 4.3% caused by sweating at rest for 6 hr in the heat with and without fluid ingestion reduced $\dot{V}O_{2max}$ measured in 46°C heat by 10% and 27%, respectively. Differences in heat stress and dehydration protocols probably account for the discrepant results. Additionally, $\dot{V}O_{2max}$ measured in more temperate environments such as ours is not reduced with dehydration of less than 3% body weight (31).

Paragraph Number 29 Our primary finding was that $\dot{V}O_{2max}$ was reduced 19% when measured following 45 min, compared to 15 min, of submaximal cycling in the heat during which substantial CVdrift occurred. The reduction following 45 min was not the result of lack of effort or failure to achieve $\dot{V}O_{2max}$, or a $\dot{V}O_{2peak}$ for these conditions. Individual subjects attained a HR_{max} within 5 bpm

of the control HR_{max} (189 ± 6 bpm) on all experimental tests. Furthermore, mean

HR_{max} during the experimental tests was not different from control HR_{max} for the

tests following 15 min (191± 5 bpm), and was significantly greater than control

HR_{max} in the tests following 45 min (194 ± 5 bpm) of submaximal exercise. The

same or higher HR_{max} during the experimental trials strongly suggests

cardiovascular capacity had been attained. Mean RPE at the point of exhaustion

during the graded exercise tests was near 19, indicating a similar, near-maximal

effort was given under all conditions. Blood lactate accumulation, ventilation and

RER were lower in the experimental tests than control values, but this more likely

reflects reduced absolute power output at $\dot{V}O_{2max}$ rather than lack of effort.

   Paragraph Number 30 A limitation to the current design is that there was

no baseline condition without CVdrift present. Thus, ascertaining whether CVdrift

caused the reduction in $\dot{V}O_{2max}$ is not possible from these findings. However, the

markedly lower $\dot{V}O_{2max}$ following 45 min compared to 15 min of submaximal

exercise indicates that cardiovascular alterations or some other changes that

develop over time are at least associated with reduced $\dot{V}O_{2max}$. Although we are not

the first to report reduced $\dot{V}O_{2max}$ following prolonged exercise, we are the first that

we are aware of to show that $\dot{V}O_{2max}$ is reduced over the same time interval that

CVdrift occurs. The change in $\dot{V}O_{2max}$ in our study was greater than that in several

previous studies in which decreases in $\dot{V}O_{2max}$ of 5-12% following prolonged

strenuous exercise in thermoneutral conditions were reported (10,29,30).

However, in these studies, $\dot{V}O_{2max}$ was not measured at the same points in time as

the variables characterizing CVdrift. The initial $\dot{V}O_{2max}$ was measured on a

different day and the $\dot{V}O_{2max}$ after exercise was usually measured following a rest

period. A period of rest would alter some of the conditions that appear to contribute

to CVdrift, such as hyperthermia. Thus, it is uncertain whether the altered $\dot{V}O_{2max}$

accurately reflected the effect of CVdrift. In addition, during prolonged,

continuous exercise in a hot environment, in which there is greater hyperthermia and CVdrift (13) than in a thermoneutral environment, the metabolic consequences of cardiovascular drift may be greater. The greater change in $\dot{V}O_{2max}$ following prolonged exercise in our study than in previous studies in thermoneutral conditions may reflect the effects of greater heat stress and hyperthermia.

Paragraph Number 31 Greater hyperthermia at $\dot{V}O_{2max}$ following 45 min compared to 15 min of submaximal exercise could have contributed to the reduction in $\dot{V}O_{2max}$. T_{re} and T_b at $\dot{V}O_{2max}$ were higher by ~1°C, and T_{sk} was higher by 0.3°C, following 45 compared to 15 min of submaximal exercise. The 19% reduction in $\dot{V}O_{2max}$ following 45 min of exercise in the heat in our study is consistent with the results of other studies in which large (16-27%) decreases in $\dot{V}O_{2max}$ have been observed following prior exercise in severe heat stress that markedly elevated both core and skin temperatures (2,23,24). Likewise, the lack of reduction in $\dot{V}O_{2max}$ following 15 min of submaximal exercise at 35°C in which the increase in T_{re} was much smaller than following 45 min is consistent with studies that have found only small (3-8%) (24,27,32) or no change (26,36) in $\dot{V}O_{2max}$ after brief heat exposure without prior exercise or preheating and with only modest increases in core body temperature.

Paragraph Number 32 The cardiovascular and/or metabolic alterations through which $\dot{V}O_{2max}$ was reduced following 45 min compared to 15 min of submaximal exercise in the heat cannot be determined from the data collected in this study. HR_{max} was not reduced and, in fact, was significantly higher by an average of 3 beats·min^{-1}. Therefore, the decrease in $\dot{V}O_{2max}$ following 45 min was due to lower arteriovenous oxygen difference [(a-$\bar{v}$)O_2] or SV, as reflected by the reduction in O_2 pulse. Assuming that the (a-$\bar{v}$)O_2 diff was not reduced (14,28,36), the lower O_2 pulse accompanying reduced $\dot{V}O_{2max}$ would reflect reduced maximal SV and $\dot{Q}$. This deduction is consistent with the findings of González-Alonso and

Calbet (14) who found that the reduction in $\dot{V}O_{2max}$ with heat stress was due to a reduction in MAP, SV and $\dot{Q}$. Lower $\dot{Q}_{max}$ was associated with lower leg blood flow and reduced oxygen delivery to the active muscles, limiting $\dot{V}O_{2max}$. The cause of the reduced SV was uncertain. Reduced SV could be caused by 1) greater cutaneous vasodilation and increased venous volume, which reduces central blood volume, ventricular filling pressure and end-diastolic volume (28); 2) a slightly greater degree of dehydration and reduced plasma volume, which would contribute to lowered filling pressure and end-diastolic volume; and, 3) slightly greater tachycardia, which would reduce ventricular filling time and may contribute to reduced end-diastolic volume (12).

   Paragraph Number 33 Our data do not provide new insight into the mechanism underlying CVdrift, but suggest that if exercise intensity is increased up to the intensity eliciting HR_{max} after CVdrift has occurred, the reduced SV present at the end of 45 min of submaximal exercise in the heat apparently cannot be overcome and restored to the control level. This could mean 1) that factors other than increased HR contributed to the reduction in SV during prolonged exercise and that these factors or conditions persisted during maximal exercise or 2) that as intensity was increased to $\dot{V}O_{2max}$, the expected increases in myocardial contractility and vasoconstriction in the splanchnic, non-active muscle and skin vascular beds that maintain or increase SV were inadequate to increase the reduced SV to the control level.

   Paragraph Number 34 Our data have implications for the use of HR to prescribe exercise intensity. This study is the first that we are aware of to evaluate whether the strong link between HR and relative metabolic intensity, demonstrated during short-term exercise (8,35), persists during prolonged, constant-rate exercise during which submaximal $\dot{V}O_2$ remains nearly constant, but HR rises progressively, over time. We found that the increase in HR did reflect an increase in relative

metabolic intensity, because $\dot{V}O_{2max}$ decreased over time. While not exactly proportional, the changes in %HRR and %$\dot{V}O_2R$ were quite similar (Table 3 and Figure 2). Thus, these data provide support for the practice of using HR as a marker of change in relative metabolic intensity during prolonged exercise in the heat in which a progressive rise in HR occurs over time.

     Paragraph Number 35 We conclude CVdrift during 45 min of continuous exercise in a hot environment is associated with decreased $\dot{V}O_{2max}$ and increased relative metabolic intensity. The results support the validity of using changes in HR to reflect changes in relative metabolic intensity under conditions like those imposed in this study in which CVdrift occurs.

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FIGURE LEGENDS

Figure 1: Changes in mean (±SEM) heart rate (HR) and stroke volume (SV) between 15 and 45 min of cycling at ~63% of the control $\dot{V}O_{2max}$. * Change significant at $p < 0.05$.

Figure 2: Relation of change in percent oxygen uptake reserve (%$\dot{V}O_2R$) and change in percent heart rate reserve (%HRR) [%$\Delta\dot{V}O_2R = 1.24\ \Delta$%HRR + 0.46, r = 0.71, SEE = 6.7%, $p < 0.05$] between 15 and 45 min of cycling at ~63% of the control $\dot{V}O_{2max}$.
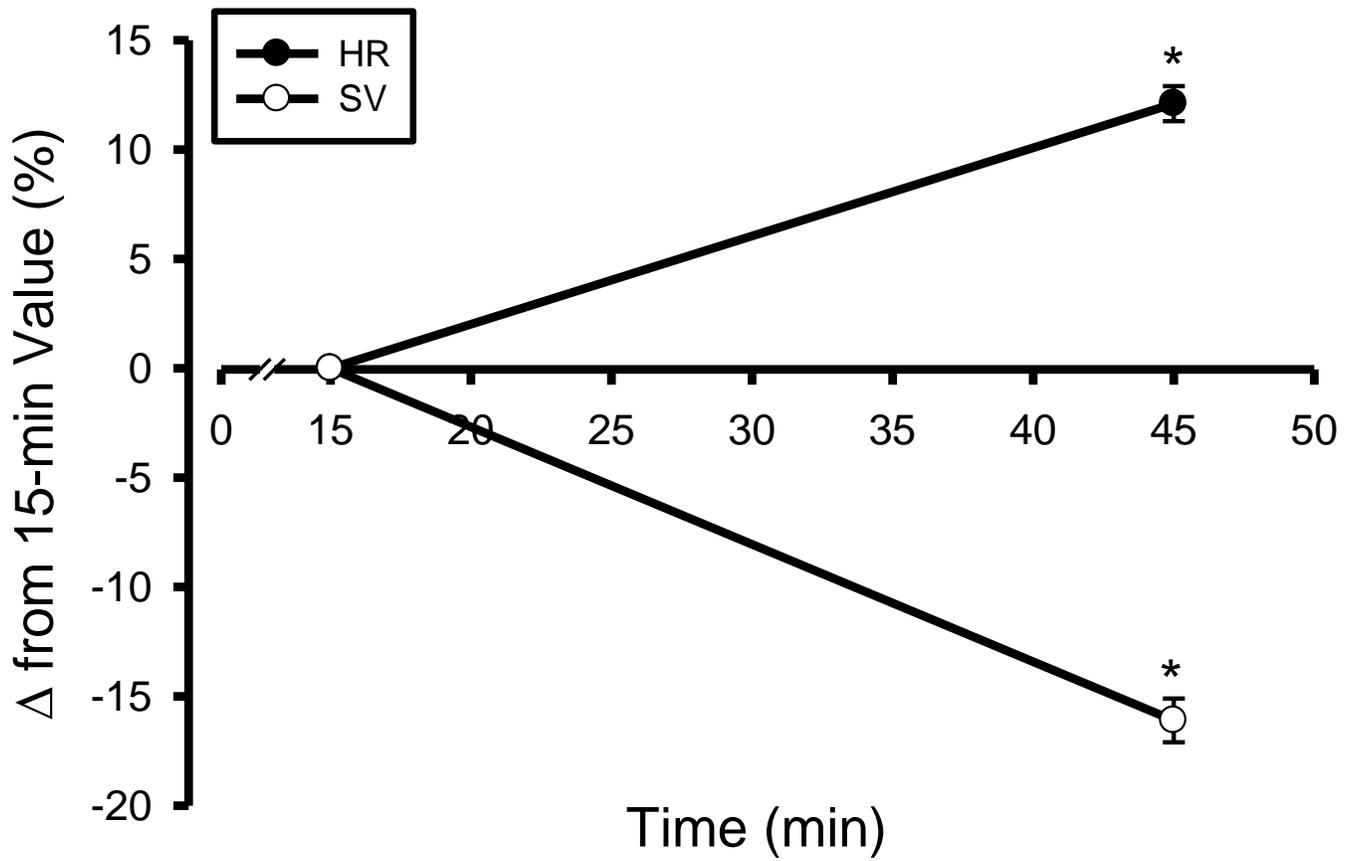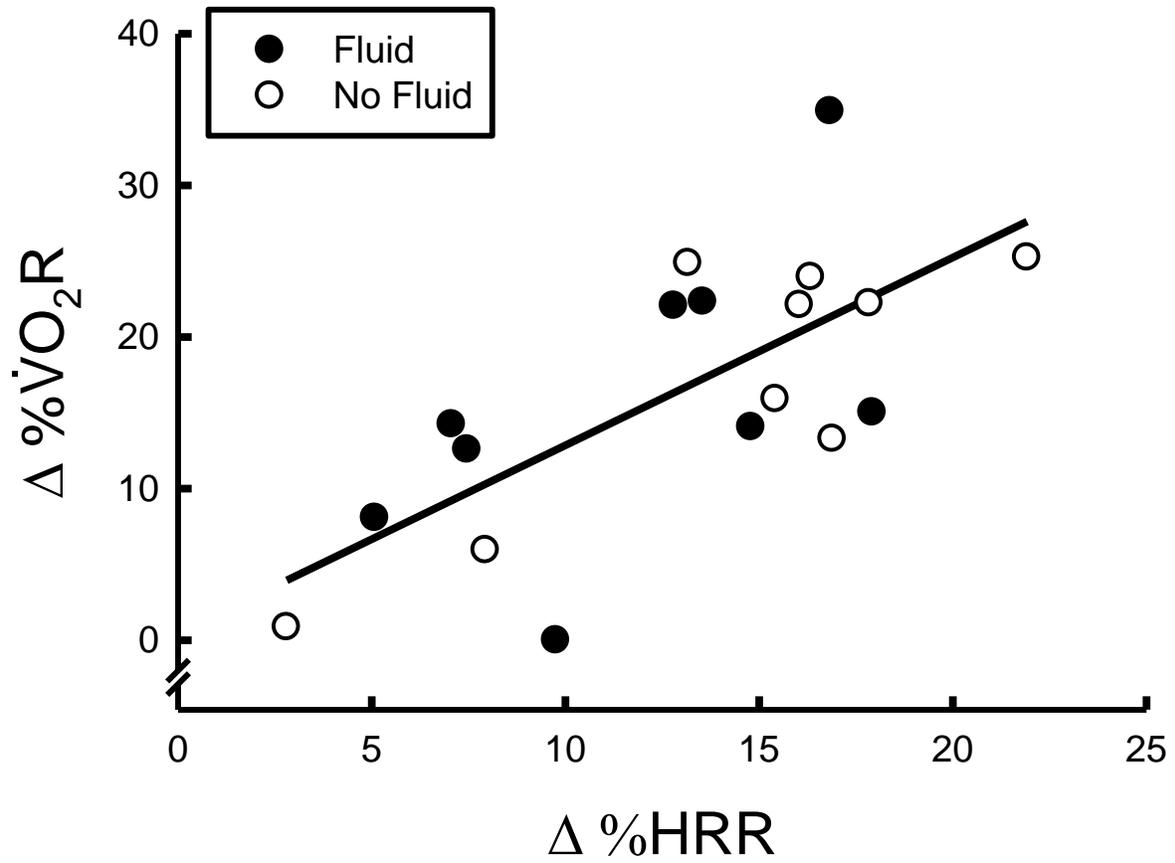
Figure 1.

Figure 2.

Table 1. Responses during submaximal exercise with data from fluid and no fluid

conditions combined (mean ± SD).

Variable	Time	
	15-min	45-min
$\dot{V}O_2$ (L·min^{-1})	2.69 ± 0.19	2.74 ± 0.19 *
$\dot{V}O_2$ (% control $\dot{V}O_{2max}$)	62.7 ± 4.0	63.7 ± 3.9 *
$\dot{Q}$ (L·min^{-1})	18.1 ± 1.3	17.1 ± 1.6 *
SV (mL·min^{-1})	120.5 ± 12.2	101.0 ± 10.3 *
HR (beats·min^{-1})	151.1 ± 8.5	169.3 ± 9.7 *
O_2 pulse (mL·beat^{-1})	17.9 ± 1.9	16.2 ± 1.7 *
MAP (mm Hg)	100.3 ± 8.1	100.3 ± 10.5
SVR (dyn·cm·s^{-5})	5.6 ± 0.6	5.9 ± 0.9 *
Blood lactate (mmol·L^{-1})	2.4 ± 1.0	2.6 ± 1.1 *
ΔPV from rest (%)	-6.1 ± 2.1	-8.2 ± 3.2 *
Epinephrine (ng·mL^{-1})	6.1 ± 3.4	6.7 ± 3.8
Norepinephrine (ng·mL^{-1})	1.4 ± 0.9	2.3 ± 0.7 *
T_{re} (°C)	37.9 ± 0.3	38.9 ± 0.3 *
$\overline{T}_{sk}$ (°C)	35.9 ± 0.4	36.2 ± 0.5 *
$\overline{T}_b$ (°C)	37.6 ± 0.3	38.6 ± 0.5 *
RPE	12.2 ± 0.5	14.3 ± 1.6 *

$\dot{V}O_2$ = oxygen uptake, $\dot{Q}$ = cardiac output, SV = stroke volume, HR = heart rate,

MAP = mean arterial pressure, SVR = systemic vascular resistance, T_{re} = rectal

temperature, $\overline{T}_{sk}$ = mean skin temperature, $\overline{T}_b$ = mean body temperature, RPE =

rating of perceived exertion, *Significantly different from 15-min value at $p < 0.05$.

Table 2. Responses to maximal exercise during a control graded exercise test and following 15 min or 45 min of submaximal exercise with data from fluid and no fluid conditions combined.

		Time	
Variable	Control	15-min	45-min
$\dot{V}_E$ (STPD, $L \cdot min^{-1}$)	137.2 ± 10.8	$129.5 \pm 9.6\ ^{\dagger}$	$111.8 \pm 14.5\ *^{\dagger}$
$\dot{V}O_2$ ($L \cdot min^{-1}$)	4.3 ± 0.5	4.4 ± 0.6	$3.6 \pm 0.4\ *$
$\dot{V}O_2$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	60.4 ± 8.6	61.2 ± 8.5	$49.4 \pm 6.0\ *$
RER	1.14 ± 0.04	$1.04 \pm 0.03^{\dagger}$	$1.03 \pm 0.04\ *^{\dagger}$
RPE	19.1 ± 0.8	18.9 ± 1.0	19.0 ± 0.9
HR (beats·min^{-1})	189 ± 5.7	191 ± 5	$194 \pm 5\ *$
O_2 pulse (mL·beat^{-1})	22.9 ± 2.8	23.1 ± 2.9	$18.4 \pm 2.1\ *$
Blood lactate (mmol·L^{-1})	8.5 ± 1.4	$7.0 \pm 1.0^{\dagger}$	$5.2 \pm 1.7\ *^{\dagger}$
ΔPV from rest (%)	—	-13.7 ± 3.3	-11.8 ± 3.1
Epinephrine (ng·mL^{-1})	—	5.7 ± 3.8	$7.8 \pm 3.7\ *$
Norepinephrine (ng·mL^{-1})	—	5.1 ± 1.8	$4.3 \pm 1.1\ *$
T_{re} (°C)	—	38.2 ± 0.4	$39.2 \pm 0.3\ *$
$\overline{T}_{sk}$ (°C)	—	36.0 ± 0.7	36.1 ± 0.8
$\overline{T}_b$ (°C)	—	37.9 ± 0.4	$38.8 \pm 0.3\ *$
Δ Body Mass (%)	—	-0.9 ± 0.7	$-1.4 \pm 1.3\ *$
Test Duration (min)	11.9 ± 3.5	10.0 ± 2.0	$6.5 \pm 2.3\ *^{\dagger}$
Power Output (watts)	333 ± 45	$300 \pm 44^{\dagger}$	$253 \pm 41\ *^{\dagger}$

$\dot{V}_E$ = minute ventilation, $\dot{V}O_{2max}$ = maximal oxygen uptake, RER = respiratory exchange ratio, RPE = rating of perceived exertion, HR = heart rate, ΔPV = plasma volume change from rest, T_{re} = rectal temperature, $\overline{T}_{sk}$ = mean skin temperature, $\overline{T}_b$ = mean body temperature, *Significantly different from 15-min value at $p < 0.05$. †Significantly different from control value at $p < 0.05$.

Table 3. Measures of exercise intensity during submaximal exercise based on
maximal values obtained during the control graded exercise test (GXT) and during
the GXTs following each experimental trial.

Variable	Maximal values based on control GXT		Maximal values based on GXTs following experimental trials	
	15-min	45-min	15-min	45-min
% $\dot{V}O_{2max}$	62.7 ± 4.0	63.7 ± 3.9 *	61.7 ± 5.7	77.7 ± 7.4 *
% HR_{max}	80.0 ± 3.7	89.6 ± 3.9 *	79.2 ± 3.9	87.4 ± 4.2 *
% $\dot{V}O_2R$	60.2 ± 4.1	61.2 ± 3.8	59.5 ± 5.8	76.0 ± 7.9 *
% HRR	69.0 ± 5.5	84.0 ± 6.0 *	68.0 ± 5.8	80.9 ± 6.1 *

$\dot{V}O_{2max}$ = maximal oxygen uptake, HR_{max} = maximal heart rate, %$\dot{V}O_2R$ = percent
of maximal oxygen uptake reserve, %HRR = percent of maximal heart rate reserve.
 *Significantly different from 15-min value at $p < 0.05$.