

Effects of marked hyperthermia with and without dehydration on $\dot{V}O_2$ kinetics during intense exercise

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Nybo, Lars, Thorbjørn Jensen, Bodil Nielsen, and José González-Alonso. Effects of marked hyperthermia with and without dehydration on $\dot{V}O_2$ kinetics during intense exercise. *J Appl Physiol* 90: 1057–1064, 2001.—This study determined whether marked hyperthermia alone or in combination with dehydration reduces the initial rate of rise in O_2 consumption ($\dot{V}O_2$ on-kinetics) and the maximal rate of O_2 uptake ($\dot{V}O_{2\max}$) during intense cycling exercise. Six endurance-trained male cyclists completed four maximal cycle ergometer exercise tests (402 ± 4 W) when euhydrated or dehydrated (4% body wt) with normal (starting esophageal temperature, $37.5 \pm 0.2^\circ\text{C}$; mean skin temperature, $\sim 31^\circ\text{C}$) or elevated (+1 and $+6^\circ\text{C}$, respectively) thermal strain. In the euhydrated and normal condition, subjects reached $\dot{V}O_{2\max}$ (4.7 ± 0.2 l/min) in 228 ± 34 s, with a mean response time of 42 ± 2 s, and fatigued after 353 ± 39 s. Hyperthermia alone or in combination with dehydration reduced mean response time (17–23%), $\dot{V}O_{2\max}$ (16%), and performance time (51–53%) (all $P < 0.01$) but did not alter the absolute response time (i.e., the time to reach 63% response in the control trial, 3.2 ± 0.1 l/min, 42 s). Reduction in $\dot{V}O_{2\max}$ was accompanied by proportional decline in O_2 pulse and significantly elevated maximal heart rate (195 vs. 190 beats/min for hyperthermia vs. normal). Preventing hyperthermia in dehydrated subjects restored $\dot{V}O_{2\max}$ and performance time by 65 and 50%, respectively. These results demonstrate that impaired high-intensity exercise performance with marked skin and internal body hyperthermia alone or in combination with dehydration is not associated with a diminished rate of rise in $\dot{V}O_2$ but decreased $\dot{V}O_{2\max}$.

maximal heart rate; hydration; core temperature; skin temperature, oxygen uptake

DURING EXERCISE IN THE HEAT, pronounced dehydration and hyperthermia can, in some conditions, reduce cardiac output, skin blood flow, visceral blood flow, skeletal muscle blood flow, mean arterial pressure (9, 11, 12, 17, 23, 26, 28, 34), as well as maximal O_2 consumption ($\dot{V}O_{2\max}$) (6, 25). It is unclear, however, whether the initial rate of rise in O_2 consumption ($\dot{V}O_2$ on-kinetics) is also compromised in conditions of marked dehydration and hyperthermia. The possibility exists that $\dot{V}O_2$ on-kinetics is either attenuated, unaltered, or potenti-

ated, depending on the effects of high body temperature and dehydration on tissue and organ blood flow, O_2 extraction, and enzyme activity (Q_{10} effect). Evidence during moderate-intensity exercise suggests that noticeable muscle and core hyperthermia has no effect on either $\dot{V}O_2$ on-kinetics (22) or $\dot{V}O_2$ slow component (9, 10), due largely to the compensatory increase in exercising muscle O_2 extraction (9, 10). However, during high-intensity exercise, $\dot{V}O_2$ on-kinetics could change with hyperthermia and/or dehydration if O_2 delivery to contracting skeletal muscle is substantially altered, as suggested by studies manipulating inspiratory O_2 fraction, exercise position, or blood volume distribution (applying lower body negative pressure; for recent review see Ref. 15). On the other hand, the relative contribution of dehydration and hyperthermia to the decline in $\dot{V}O_{2\max}$ with marked dehydration and hyperthermia remains elusive, as results in this area are controversial. $\dot{V}O_{2\max}$ has been shown to be reduced (21, 25, 32), unaltered (26, 29, 37), or increased (3) when subjects exercise under different levels of hyperthermia with and without dehydration, and it appears that dehydration in the absence of thermal stress induces only minor (4) or no reductions in $\dot{V}O_{2\max}$ (1, 5, 18, 31, 35).

Therefore, the purpose of this study was twofold: 1) to determine whether $\dot{V}O_2$ on-kinetics would be blunted in conditions of marked dehydration and hyperthermia [i.e., 4% body wt loss; esophageal temperature (T_{es}) = $+1^\circ\text{C}$ and mean skin temperature (T_{sk}) = $+6^\circ\text{C}$] expected to impair $\dot{V}O_{2\max}$, and 2) to determine to what extent the hampered maximal aerobic capacity is related to the independent effects of dehydration and hyperthermia. We speculated that the $\dot{V}O_2$ on-response could be attenuated when hyperthermic and dehydrated subjects initiate an intense exercise bout. Furthermore, we hypothesized that the impairment of high-intensity exercise performance with dehydration and hyperthermia is largely related to effects of hyperthermia on reducing $\dot{V}O_{2\max}$. There are many possible heat strain conditions resulting from different levels of dehydration and hyperthermia. We chose to study

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large differences in hydration status and body temperature, which could represent physiological conditions experienced by athletes performing in hot environments without fluid replacement, compared with cool environments with full fluid replacement.

METHODS

Subjects. Six endurance-trained male cyclists participated in this study. They had a mean (\pm SD) age of 24 ± 2 yr, body weight of 73.3 ± 6.9 kg, and height of 182 ± 5 cm. Maximal heart rate (HR_{\max}) and $\dot{V}O_{2\max}$ determined during an incremental protocol were 189 ± 8 beats/min and 4.69 ± 0.46 l/min (64.5 ± 3.0 ml·kg⁻¹·min⁻¹), respectively. The subjects were fully informed of the risks and discomforts associated with the experiments before they gave their informed written consent to participate. All subjects completed six practice trials to adapt to the maximal tests and the hot environment. On the last practice day, the subjects performed two maximal tests separated by 1 h, revealing the same $\dot{V}O_{2\max}$, HR_{\max} , and performance time when environmental and hydration conditions were unchanged. Furthermore, $\dot{V}O_{2\max}$ and HR_{\max} attained during the tests with constant workload were similar to the values determined during the tests with incremental protocol.

Experimental design. On two occasions separated by 5–7 days, the subjects completed four counterbalanced maximal exercise tests on a cycle ergometer (Monark 829E) (see Fig. 1). Each maximal test was separated from previous exercise by a 1-h interval consisting of 45 min of rest, 12 min of light cycling ($\sim 50\%$ $\dot{V}O_{2\max}$), and 3 min of rest while the subject was seated on the cycle ergometer. The maximal tests were performed with either a normal [starting $T_{es} = 37.5 \pm 0.2^\circ\text{C}$ (\pm SE) and $T_{sk} = 30.8 \pm 0.6^\circ\text{C}$; normal] or a hyperthermic ($T_{es} = 38.5 \pm 0.2^\circ\text{C}$ and $T_{sk} = 37.0 \pm 0.2^\circ\text{C}$; hyper) condition. Core and skin temperatures were manipulated by changing the temperature of the water perfusing a jacket that was in contact with the skin of the trunk and arms (water temperature: 14°C in normal and 44°C in hyper). The subjects wore the perfused jacket throughout the last 15 min of the resting period, during the 12 min of light cycling, and during the maximal tests. In addition, to lower the elevated body temperature from previous exercise and to ensure a normal starting body temperature in normal trials, subjects were immersed in 15°C water for 15 min. In the hyper trials, heat stress was increased during the resting and light exercise periods by having the subjects wear rain trousers. The exercise tests were performed until exhaustion at a work intensity that exhausted the subjects within 5–8 min (402 ± 4 W; range 365–450 W) and elicited $\dot{V}O_{2\max}$ in 3–5 min under normal environmental and hydration conditions (pretests). During the maximal tests, $\dot{V}O_2$, heart rate, and body temperature were measured continuously, whereas blood samples

were withdrawn at the point of exhaustion, and body weight was recorded immediately after the tests.

On a given day, the maximal tests were preceded by a 2-h exercise bout at $\sim 50\%$ of $\dot{V}O_{2\max}$ in the heat ($\sim 37^\circ\text{C}$, 15–20% relative humidity), in which the subject's hydration status was altered. On 1 day [dehydration (DH) trial], the subjects only ingested 0.3 liter of a concentrated carbohydrate-electrolyte solution and became dehydrated by $4.0 \pm 0.3\%$ of their body weight. On the other day [euhydration (EU) trial], they ingested 3.0 ± 0.2 liters of diluted carbohydrate-electrolyte solution, thereby maintaining their hydration status. The solution, which contained 100 g of carbohydrate on both days, was divided into eight equal aliquots and ingested every 15 min during the 2-h exercise bout.

$\dot{V}O_2$, O_2 kinetics, and heart rate. Pulmonary $\dot{V}O_2$, CO_2 production, and ventilation were measured on-line, breath by breath, with Medgraphics cardiopulmonary exercise testing system CPX/D (Saint Paul, MN). To characterize $\dot{V}O_2$ on-kinetics, a monoexponential function of time [$f(t)$] with the formula

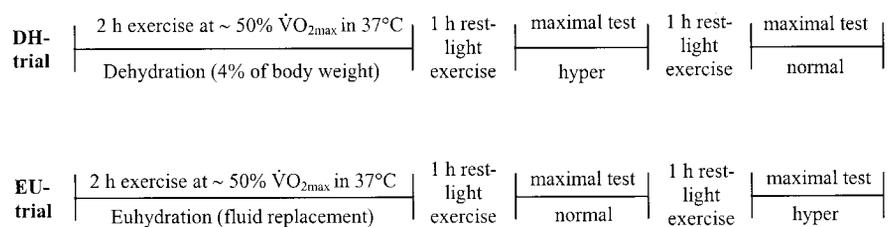
$$f(t) = \dot{V}O_{2\text{baseline}} + \Delta\dot{V}O_2 * [1 - e^{-(t-T_d)/\tau}]$$

where $\dot{V}O_{2\text{baseline}}$ is the $\dot{V}O_2$ during the minute before starting the maximal exercise bouts and $\Delta\dot{V}O_2$ is the increase at time t above that at baseline, was fitted to the individual data, and parameter values [delay constant (T_d) and time constant (τ)] that yielded the lowest sum of squared residuals were determined (36). No attempt was made to fit a mathematical model to the initial phase because of the limited number of data points during the first 10–15 s of exercise (15). Furthermore, the application of a two-exponential model to the raw $\dot{V}O_2$ data did not improve the mathematical fitting (both mono- and two-exponential models, $r = 0.94 \pm 0.01$), thus rendering the basis for selecting the simplest fitting model. In contrast to previous studies examining $\dot{V}O_2$ kinetics during heavy exercise (2, 19, 22), it was only feasible to perform one maximal trial per exercise condition in the present study. Mean response time (τ) was then calculated by solving the above equation with respect to the time necessary to reach 63% (corresponding to time constant of monoexponential response; τ) of the difference between baseline (rest) and the maximal response (plateau corresponding to $\dot{V}O_{2\max}$). Heart rate was recorded every 5 s with a Polar Sports Tester (Polar Electro). O_2 pulse ($O_{2\text{pulse}}$) was calculated by dividing $\dot{V}O_2$ by heart rate.

Core and skin temperature. T_{es} was measured with a thermocouple (MOV-A, Ellab, Copenhagen, Denmark) inserted through the nasal passage at a distance equal to one-fourth of the subject's height (33). T_{sk} was calculated from the skin temperatures (thermocouple A-H3, Ellab) measured at six sites (i.e., back, chest, upper arm, forearm, thigh, and calf) using the weighting method of Hardy and DuBois (16). The esophageal and skin thermocouples were connected to a recorder (CTF 9008 Precision Thermometer and Fo-Value

Fig. 1. Sequence of the experimental protocol whereby subjects first cycled for 2 h to become dehydrated (DH) or remain euhydrated (EU, by fluid replacement) and then performed 2 intense cycle ergometer exercise tests until exhaustion: 1 with normal and the other with elevated thermal strain [hyperthermia (hyper)]. The maximal tests were separated from previous exercise by 1-h interval consisting of 45 min of rest, 12 min of light cycling [50% maximal O_2 consumption ($\dot{V}O_{2\max}$)], and 3 min of seated rest on the cycle ergometer.

Experimental protocol



Computer, Ellab), and temperatures were registered every 30 s with an accuracy of 0.1°C. Muscle temperature was measured in the vastus lateralis in one subjects with a needle probe (model MKA-A, Ellab) inserted 3 cm into the muscle.

Blood analysis. All resting blood samples were withdrawn from an antecubital vein after the subject had been seated for at least 15 min. Hemoglobin and hematocrit were determined in duplicate using an ABL 510 analyzer (Radiometer, Copenhagen, Denmark). Percent changes in blood volume and plasma volume were calculated by using the equations of Dill and Costill (7). Lactate and blood glucose concentrations were measured by using a glucose and lactate YSI model 2700 analyzer (Yellow Springs Instruments). Plasma osmolality was determined by the freezing point-depression technique (advanced osmometer model 3D3, Advanced Instruments), whereas plasma norepinephrine and epinephrine were determined by using a RIA kit (KatCombi RIA, Biotech-IgG, Copenhagen, Denmark).

Statistical analysis. One- and two-way ANOVA with repeated measures were performed to test significance among the different trials. After a significant *F* test, pairwise differences were identified by using Tukey's honestly significant difference post hoc procedure. When appropriate, significant differences were also identified by using Student's paired *t*-test. The significance level was set at $P < 0.05$. Data are presented as means \pm SE.

RESULTS

Hydration status. Hydration status at the beginning of the 2 testing days (DH vs. EU) was not different, as indicated by similar body weights (73.3 ± 3.0 vs. 73.2 ± 2.9 kg, respectively), plasma osmolality (285 ± 1 vs. 286 ± 1 mosmol/kgH₂O, respectively), and hemoglobin concentration (14.8 ± 0.3 g/dl on both days). In DH, body weight declined to 70.7 ± 2.8 kg ($4.0 \pm 0.3\%$ body wt loss), whereas plasma osmolality rose to 297 ± 3 mosmol/kgH₂O, and hemoglobin concentration increased to 15.3 ± 0.3 g/dl, reflecting a $4.1 \pm 1.1\%$ blood volume reduction. In EU, body weight, plasma osmolality, and hemoglobin concentration remained unchanged (Table 1). No differences in hydration were detected between hyper and normal trials on the respective days (Table 1).

Core and skin temperature. During the four maximal trials, T_{es} increased progressively throughout exercise, whereas T_{sk} remained constant (Fig. 2). The rate of increase in T_{es} was similar in the four trials ($0.18^\circ\text{C}/\text{min}$), thereby maintaining the $\sim 1^\circ\text{C}$ higher T_{es} in hyper vs. normal. However, because of the longer exercise times in normal, T_{es} rose over a longer period, and at exhaustion the difference in T_{es} between EU-normal and EU-hyper, therefore, decreased to 0.3°C (38.7 ± 0.3 vs. $39.0 \pm 0.2^\circ\text{C}$) and was no longer significant, whereas the difference between DH-normal and DH-hyper declined to 0.5°C (38.5 ± 0.2 vs. $39.0 \pm 0.2^\circ\text{C}$; $P < 0.05$). T_{sk} was at all time points $\sim 6^\circ\text{C}$ higher ($P < 0.01$) in the hyper trials compared with the normal trials (see Fig. 2B).

$\dot{V}O_2$ and performance time. $\dot{V}O_2$ before (baseline) and during the first 60 s of exercise was similar in all trials (Fig. 3A and Fig. 4). However, after 60 s of exercise, $\dot{V}O_2$ was significantly lower in EU-hyper and DH-hyper

Table 1. *Hematologic parameters at rest and during intense cycle ergometer exercise with euhydration and dehydration under normal or elevated thermal strain*

Variables	Euhydration		Dehydration	
	Normal	Hyperthermia	Hyperthermia	Normal
Hemoglobin, g/dl	14.8 ± 0.3	14.8 ± 0.3	$15.3 \pm 0.3^*$	$15.3 \pm 0.3^*$
Hematocrit, %	45.2 ± 0.6	44.8 ± 0.6	46.3 ± 0.6	$47.0 \pm 0.6^*$
Blood volume, %change	0.0 ± 0.0	0.1 ± 0.4	$-4.5 \pm 0.3^*$	$-3.7 \pm 0.5^*$
Osmolality, mosmol/kgH ₂ O	283 ± 1	285 ± 1	$297 \pm 4^*$	$298 \pm 3^*$
Lactate, mmol/l	5.9 ± 0.8	6.0 ± 0.8	5.6 ± 0.6	5.1 ± 0.6
Glucose, mmol/l	3.5 ± 0.2	3.9 ± 0.4	4.4 ± 0.6	4.9 ± 0.5
Epinephrine, nmol/l	8.0 ± 1.3	7.7 ± 1.2	6.1 ± 1.5	6.0 ± 1.4
Norepinephrine, nmol/l	27.7 ± 5.6	24.7 ± 5.0	18.8 ± 1.1	17.8 ± 5.8

Values are means \pm SE for 5 subjects. Blood volume is expressed as percent change from euhydration normal. Hemoglobin, hematocrit, and osmolality were measured before exercise while subjects were resting on the cycle ergometer (values shown) and at exhaustion. Values at exhaustion showed a similar pattern of response as those at rest but were also influenced by different exercising time. Lactate, glucose, epinephrine, and norepinephrine concentrations were only measured at exhaustion. *Significantly different from euhydration normal and euhydration-hyperthermia ($P < 0.05$).

compared with EU-normal ($P < 0.05$; Fig. 3A). At 156 ± 17 s (exhaustion in the shortest trial), $\dot{V}O_2$ was reduced by 0.44–0.45 l/min in the hyper trials, and the total amount of O₂ consumed until this time was 0.6 liter lower in EU-hyper and DH-hyper compared with EU-normal ($P < 0.01$; Table 2). $\dot{V}O_{2\max}$ was equally reduced by $16 \pm 1\%$ in the two hyper trials, and performance time was shortened by approximately one-half compared with that in EU-normal ($51 \pm 6\%$ reduction in EU-hyper and $53 \pm 6\%$ in DH-hyper; both $P < 0.01$). Preventing hyperthermia in dehydrated subjects (DH-normal) restored two-thirds of the decline in $\dot{V}O_{2\max}$ and almost one-half of the reduction in performance time. However, compared with EU-normal, both $\dot{V}O_{2\max}$ and performance time with dehydration alone were significantly reduced by 5 ± 2 and $26 \pm 8\%$ ($P < 0.05$), respectively (Table 2).

$\dot{V}O_2$ on-kinetics. $\dot{V}O_2 \tau$, defined as the time necessary to reach 63% of the rise in $\dot{V}O_2$ between baseline and the maximal response, was significantly shorter in the two hyper trials compared with EU-normal (Table 3). However, this was due to the reduced $\dot{V}O_{2\max}$ and not to a faster rise in $\dot{V}O_2$ in the hyper trials (63% response was reduced from 3.2 ± 0.1 l/min in EU-normal to 2.7 ± 0.1 l/min in the hyper trials, $P < 0.05$; see Fig. 3A). Therefore, the time to reach the same $\dot{V}O_2$ as the 63% response in EU-normal (3.2 ± 0.1 l/min) was calculated, showing no statistically significant differences among the four trials (absolute response time; Table 3).

Heart rate and O_2 pulse. Heart rate was 15–25 beats/min higher throughout exercise in the hyper trials compared with EU-normal ($P < 0.05$; Fig. 3B).

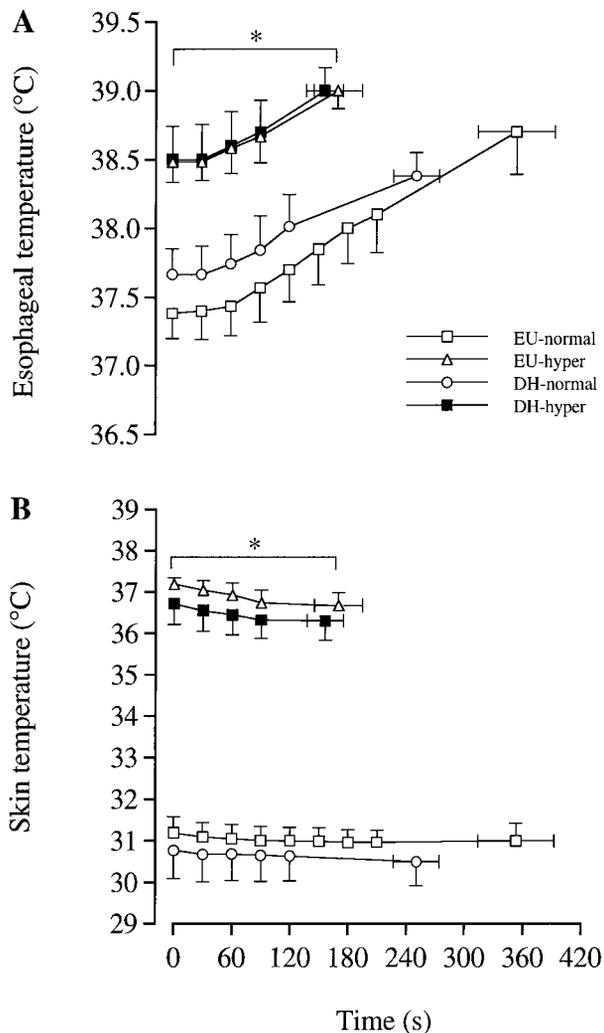


Fig. 2. Esophageal temperature (A) and mean skin temperature (B) responses during maximal cycle ergometer exercise at constant power output when subjects were euhydrated or dehydrated with normal or elevated thermal strain (EU-normal, EU-hyper, DH-normal, DH-hyper). Values are means \pm SE for 6 subjects. *Significantly higher than EU-normal, $P < 0.05$.

Furthermore, HR_{\max} was elevated by 5 ± 1 beats/min in the hyper trials compared with the respective trials with normal body temperatures ($P < 0.01$; Table 2). Dehydration without hyperthermia did not alter HR_{\max} . However, the attainment of HR_{\max} occurred faster in the DH condition compared with EU-normal (Fig. 3B).

O_2 pulse followed the same general pattern of response as $\dot{V}O_2$. However, O_2 pulse reached a maximum within 100 s of exercise in all trials. O_2 pulse was reduced by $17 \pm 2\%$ in the hyper trials compared with EU-normal ($P < 0.01$, Fig. 3C), which is highly correlated to the reductions in $\dot{V}O_{2\max}$ ($r^2 = 0.95\text{--}0.98$). Preventing hyperthermia in the DH condition restored most of the decline in O_2 pulse (see Table 2).

Blood and plasma variables. Blood glucose and lactate concentrations both at the beginning of the maximal tests and at exhaustion were similar in all four

conditions (Table 1). Furthermore, at exhaustion, no differences were detected in forearm venous plasma concentrations of epinephrine and norepinephrine (Table 1).

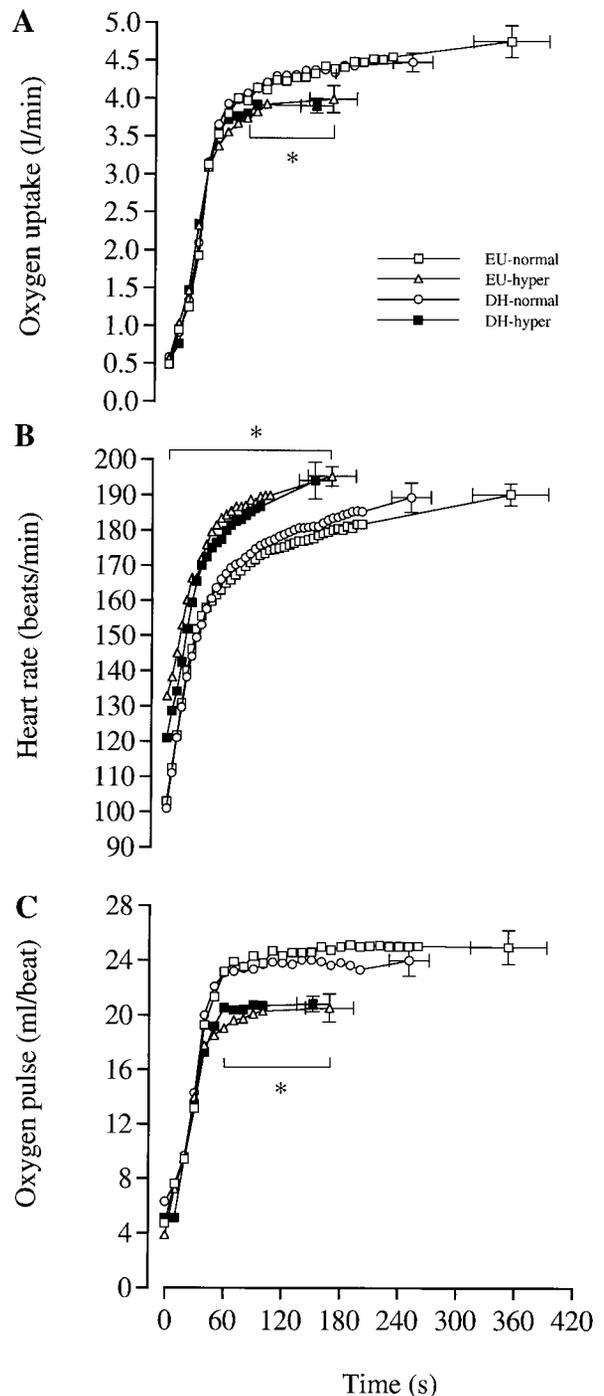


Fig. 3. O_2 consumption ($\dot{V}O_2$; A), heart rate (B), and O_2 pulse (C) responses during maximal cycle ergometer exercise at constant power output when subjects were euhydrated or dehydrated with normal or elevated thermal strain. Values are means \pm SE for 6 subjects. In EU-normal, it looks as if a plateau in $\dot{V}O_2$ is not obtained; however, this is due to the averaging effect, because all subjects maintained a plateau over the last 125 ± 23 s (range 60–230 s) of the exercise period (see Fig. 4). *Significantly different from EU-normal, $P < 0.05$.

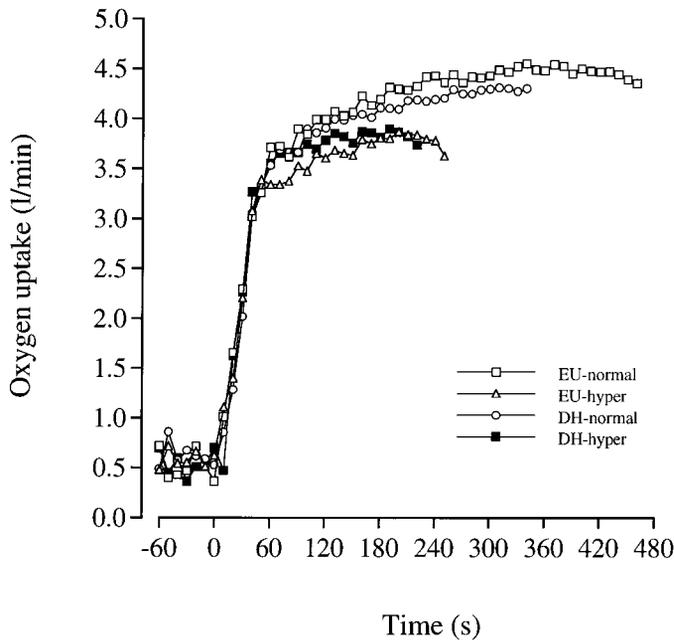


Fig. 4. $\dot{V}O_2$ response for 1 representative subject during maximal cycle ergometer exercise at constant power output when he was euhydrated or dehydrated with normal or elevated thermal strain. Of note is that a plateau in $\dot{V}O_2$ is maintained for at least 60 s in all trials.

DISCUSSION

The main finding of this study is that marked hyperthermia alone or combined dehydration and hyperthermia do not alter $\dot{V}O_2$ on-kinetics, despite the fact that they drastically reduce $\dot{V}O_{2\max}$. The observations that hyperthermia with or without dehydration resulted in similar reductions in $\dot{V}O_{2\max}$ and that prevention of hyperthermia in dehydrated subjects restored most of the decline in $\dot{V}O_{2\max}$ indicate that most of the decline in $\dot{V}O_{2\max}$ with combined dehydration and hyperthermia is associated with hyperthermia. We also observed that pronounced hyperthermia alone or in combination with dehydration led to an augmented HR_{\max} , suggesting that reduced maximal aerobic capacity was primar-

ily related to a lowering in stroke volume and/or arteriovenous O_2 difference.

Despite marked reductions in the maximal response, the initial rate of rise in $\dot{V}O_2$ was unaltered with either hyperthermia alone or combined hyperthermia and dehydration. The same interpretation of the data is reached when either a single- or a two-exponential model is used to describe the $\dot{V}O_2$ kinetics (both $r = 0.94 \pm 0.01$), as both reveal the same absolute response time (i.e., time to reach 3.2 ± 0.1 l/min, ~ 42 s). In the face of an unchanged $\dot{V}O_2$ during the initial phase of exercise, it appears that the significant reduction in τ from 42 to 33–35 s in the hyper trials compared with control only reflected the reduction in maximal response. The unaltered initial rate of rise in pulmonary $\dot{V}O_2$ in the hyper trials implies that the rate of muscle mitochondrial respiration was unchanged at the onset of exercise and that any possible reductions in O_2 delivery to the exercising leg muscles during the first minute of exercise were adequately counteracted. It is also clear that the higher muscle temperature ($\sim 1^\circ\text{C}$; see Ref. 10) in the hyper trials did not accelerate the oxidative reactions in the active muscles, corroborating previous findings during submaximal exercise (10, 11, 14, 22). However, $\dot{V}O_2$ was only similar during the initial 60 s of exercise, being thereafter significantly reduced by hyperthermia alone and combined dehydration and hyperthermia during the plateau phase.

The relative decline in $\dot{V}O_{2\max}$ (16%) with hyperthermia alone or in combination with dehydration is in agreement with the 27% $\dot{V}O_{2\max}$ reduction previously observed with hyperthermia alone (25) or combined dehydration and hyperthermia (6), but it is greater than the 3–10% $\dot{V}O_{2\max}$ decline found by others (21, 26, 32). The present observation, however, is in sharp contrast to four studies reporting that hyperthermia has no effect or increases $\dot{V}O_{2\max}$ (3, 27, 29, 37). Interestingly, Bergh and Ekblom (3) found a 2% rise in $\dot{V}O_{2\max}$ with elevated core temperature but normal skin temperature ($<31^\circ\text{C}$). The main reason for this discrepancy appears to be the difference in thermal stress between the hyper and control conditions, spe-

Table 2. Oxygen consumption, heart rate, and performance during intense cycle ergometer exercise with euhydration and dehydration under normal or elevated thermal strain

Variables	Euhydration		Dehydration	
	Normal	Hyperthermia	Hyperthermia	Normal
Performance time, s	353 \pm 39	170 \pm 25*	156 \pm 17*	251 \pm 21*†
$\dot{V}O_{2\max}$, l/min	4.74 \pm 0.21	3.99 \pm 0.18*	3.96 \pm 0.12*	4.47 \pm 0.12*†
Ventilation, l/min	179.8 \pm 6.1	171.2 \pm 6.2	167.0 \pm 6.9	167.6 \pm 3.1
RER	1.13 \pm 0.03	1.22 \pm 0.04*	1.23 \pm 0.01*	1.14 \pm 0.01†
Maximal HR, beats/min	190 \pm 3	195 \pm 3*	194 \pm 5	189 \pm 4†
O_2 pulse, ml O_2 /beat	25.0 \pm 1.2	20.5 \pm 1.0*	20.8 \pm 0.6*	24.0 \pm 0.5†
$\dot{V}O_2$ at 156 \pm 17 s, l/min	4.41 \pm 0.14	3.97 \pm 0.19*	3.96 \pm 0.12*	4.36 \pm 0.12†
Total $\dot{V}O_2$ at 156 \pm 17 s, liters	8.1 \pm 1.2	7.5 \pm 1.1*	7.5 \pm 1.2*	7.9 \pm 1.2†
HR at 156 \pm 17 s, beats/min	177 \pm 3	194 \pm 3*	194 \pm 5*	179 \pm 4†

Values are means \pm SE for 6 subjects. $\dot{V}O_2$, O_2 consumption; $\dot{V}O_{2\max}$, maximal $\dot{V}O_2$; RER, respiratory exchange ratio; HR, heart rate. *Significantly different from euhydration-normal ($P < 0.05$). †Significantly different from dehydration-hyperthermia ($P < 0.05$).

Table 3. Maximal oxygen uptake mean response time and absolute response time during intense cycle ergometer exercise with euhydration and dehydration under normal or elevated thermal strain

Subject No.	Euhydration			Dehydration			
	Normal		Hyperthermia	Hyperthermia		Normal	
	τ	τ'		τ	τ'	τ	τ'
1	41.5	33.1	41.5	26.7	46.5	37.3	41.0
2	39.2	34.9	38.7	33.6	37.0	38.9	39.1
3	35.8	37.9	45.6	38.1	44.6	39.6	41.8
4	47.5	33.2	41.7	29.2	40.4	41.1	40.8
5	50.3	37.3	41.2	38.2	46.2	42.3	45.3
6	39.0	33.8	40.2	29.6	34.7	36.9	38.2
Mean \pm SE	42.2 \pm 2.3	35.0 \pm 0.9*	41.5 \pm 1.0	32.6 \pm 2.0*	41.6 \pm 2.0	39.4 \pm 0.9	41.0 \pm 1.0

Values are expressed in s. Mean response time (τ) is defined as the time to reach 63% of the increase in $\dot{V}O_2$ from baseline to the maximal response. Absolute response time (τ') is defined as the time necessary to reach the same $\dot{V}O_2$ as the 63% response in euhydration-normal (i.e., 3.2 ± 0.1 l/min). *Significantly shorter than euhydration-normal ($P < 0.05$).

cifically whether or not internal body and skin temperatures were simultaneously elevated. The level of thermal stress that the cyclists experienced in this study was high, as core temperature was elevated by 1°C and T_{sk} was $\sim 6^\circ\text{C}$ higher throughout the exercise. This is of similar magnitude to that incurred in studies finding the greatest reductions in aerobic capacity (6, 25). In one additional subject, $\dot{V}O_{2\text{max}}$ did not decline during intense cycle ergometer exercise, even with a greatly elevated core temperature (39.8°C), as long as skin temperature was below $\sim 32^\circ\text{C}$, which further supports the notion of an interaction between elevated skin and internal body temperature. The large thermal stress experienced by subjects in this study might also explain the finding that superimposing dehydration on hyperthermia did not lead to additional reductions in $\dot{V}O_{2\text{max}}$. Restoration of most of the decline in $\dot{V}O_{2\text{max}}$ (65% restoration) when hyperthermia was prevented in the presence of dehydration in the present and other studies (4, 35) argues strongly in favor of this notion. Furthermore, studies during submaximal exercise reveal that cardiac output only declines when both core and skin temperatures are elevated (12, 29), but it is maintained when only core temperature is 1°C higher (10) or is increased when only skin temperature is elevated by $\sim 12^\circ\text{C}$ (13). Together, available evidence suggests that maximal aerobic capacity, while being sensitive to different alterations in core and skin temperature, is only markedly compromised when both skin and internal body temperatures are simultaneously elevated.

The impairment of $\dot{V}O_{2\text{max}}$ with hyperthermia alone or in combination with dehydration is tightly coupled with the parallel decline in $O_{2\text{pulse}}$ ($r^2 = 0.95\text{--}0.98$). Given its dependence on arteriovenous O_2 difference and stroke volume, the decline in $O_{2\text{pulse}}$ in the present study could potentially be ascribed to alterations in either of these factors. However, previous reports of arteriovenous O_2 difference during intense exercise indicate that hyperthermia itself does not reduce O_2 extraction (29, 37). Therefore, assuming a maximal arteriovenous O_2 difference of 170 ml O_2 /l blood in the EU trials (29, 37), the observed 16–17% reduction in

$O_{2\text{pulse}}$ and $\dot{V}O_{2\text{max}}$ with hyperthermia could be accounted for by an $\sim 26\text{-ml}$ reduction in stroke volume, leading to an ~ 4 l/min reduction in cardiac output. These estimations are consistent with the reductions in stroke volume and cardiac output observed with dehydration and hyperthermia during prolonged exercise in the heat (9–14, 23, 24). Whereas the contribution of reduced stroke volume requires experimental support, it is clear that the lower $\dot{V}O_{2\text{max}}$ with hyperthermia and combined dehydration and hyperthermia was not limited by impaired HR_{max} . On the contrary, hyperthermia increased HR_{max} by ~ 5 beats/min (195 beats/min). The observation that the HR_{max} was always close to but never >190 beats/min in all the preliminary intense training sessions, during maximal incremental exercise tests, and during the DH alone trial, strongly supports the reproducibility of this finding. The hyperthermia-induced tachycardia is a well-described phenomenon during submaximal exercise (9, 26, 29). However, to our knowledge, this is the first study to report that HR_{max} is significantly elevated with hyperthermia. The mechanism underlying the small ($<3\%$), although significant, elevation in HR_{max} with hyperthermia in this study is unclear. One possibility could be a direct effect of temperature on intrinsic heart rate, given the $0.3\text{--}0.5^\circ\text{C}$ higher T_{es} at exhaustion in the hyper trials (8, 20, 30). A second possibility could be an increased sinus-atrial node depolarization rate, secondary to reduced stretching of the heart owing to declined stroke volume (Frank-Starling mechanism). A third possibility could be an elevated sympathetic β -receptor activation of the heart in response to high body temperature and unloading of high and low baroreceptors sensing lower blood pressure and central blood volume (13, 29).

The present experimental intervention that resulted in large differences in hydration level and body temperature could represent the best and worst case scenarios (full vs. no fluid replacement) that endurance athletes could encounter during events requiring high-power outputs for several minutes during competition in hot environments. For instance, this could be the case for endurance cyclists having to sprint during or

at the end of a race. It is evident from the present results that dehydration and especially the concomitant hyperthermia have a great potential for impairing "sprinting" performance in hot environments. However, it is clear that impaired initial rate of rise in $\dot{V}O_2$ is not a limiting factor. Rather, the limitation appears to result primarily from substantial reductions in the maximal rate of aerobic ATP production, which could largely reside in the contracting skeletal muscles. During heavy exercise, it is reasonable to expect that marked hyperthermia and dehydration reduce blood flow and O_2 delivery to the active skeletal muscles (9, 10). In the hyper trials, the total amount of O_2 consumed after 156 ± 17 s of exercise (exhaustion in the shortest trial) was reduced by 0.6 liter, implying that ATP resynthesis from oxidative phosphorylation was impaired with hyperthermia alone or in combination with dehydration. Because power output was maintained constant, a proportionally greater reliance on nonoxidative ATP production might have occurred if total energy turnover had been preserved. The similar forearm venous lactate values in all conditions, despite vast differences in exercise time, suggests that glycolytic ATP production was elevated at exhaustion in the hyper compared with normal trials, which is consistent with our laboratory's recent findings during prolonged exercise in the heat (10). However, glycolytic ATP generation might have not totally compensated for the substantial reductions in $\dot{V}O_2$ in the hyper trials. In support of this, our laboratory recently observed that, despite significantly elevated muscle lactate production, total leg energy turnover was somewhat reduced when skeletal muscle blood flow and O_2 delivery declined with combined hyperthermia and dehydration during submaximal exercise (10). Whether or not early fatigue is due to reduced exercising muscle energy turnover in the hyper trials in the present study requires further elucidation. However, it is apparent that the attainment of a critically high internal body temperature was not the main factor, given that core temperature at exhaustion was $38.5\text{--}39.0^\circ\text{C}$ in all trials, which is much lower than the $\sim 40^\circ\text{C}$ associated with fatigue during submaximal exercise in hot environments (14).

In conclusion, these results demonstrate that marked skin and internal body hyperthermia in the absence or presence of dehydration do not alter the initial rate of rise in $\dot{V}O_2$. Yet hyperthermia with and without dehydration markedly impairs $\dot{V}O_{2\text{max}}$ and high-intensity performance, despite the fact that HR_{max} is significantly elevated. Preventing hyperthermia in dehydrated subjects restored most of the reductions in maximal aerobic capacity. The impairment of high-intensity exercise performance with dehydration and hyperthermia appears to be largely related to the effects of hyperthermia on reducing $\dot{V}O_{2\text{max}}$.

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