ORIGINAL RESEARCH

Stress Hormone Responses to an Ultraendurance Race in the Cold

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Objective.—Physical stress (exercise and/or environmental) activates the sympathetic-adrenal-medullary (SAM) and hypothalamic-pituitary-adrenocortical (HPA) axes. The combination of ultraendurance exercise in the cold presents a unique summated stress to the body. The purpose of this study was to assess the stress hormone response in runners, cyclists, and skiers participating in a 161-km ultraendurance race on a snow-packed course in the Alaskan wilderness.

Methods.—Forty-four athletes (20 runners, 17 cyclists, 7 skiers) competed on the same course of snow-machine trails and ice roads with each athlete carrying 7 kg of mandatory equipment. Prerace weight and blood samples were collected 2 days prior to the race start. Postrace measurements were made within 15 minutes of race finish. Hematocrit was measured, and blood samples were analyzed for levels of norepinephrine, epinephrine, adrenocorticotrophic hormone, and cortisol.

Results.—Runners lost significant weight ($-1.74 \text{ kg} \pm 1.29$) prerace to postrace. Hematocrit was maintained, and plasma volume increased minimally. Norepinephrine increased significantly prerace ($279.9 \text{ pg/mL} \pm 356.9$) to postrace ($691.7 \text{ pg/mL} \pm 422.6$) with no difference among divisions. Epinephrine did not change significantly during the race. Adrenocorticotrophic hormone ($2.40 \text{ pg/mL} \pm 2.40$ to $19.04 \text{ pg/mL} \pm 45.38$) increased significantly with no difference among divisions. Cortisol increased significantly prerace ($12.03 \text{ } \mu\text{g/dL} \pm 5.66$) to postrace ($26.69 \text{ } \mu\text{g/dL} \pm 5.77$), and postrace cortisol was significantly higher in runners vs skiers.

Conclusions.—These data suggest activation of both the SAM and HPA axes from an ultraendurance race in the cold and reveal the degree of stress hormone responses to this exhausting bout of exercise.

Key words: ultraendurance race, cold, epinephrine, norepinephrine, ACTH, cortisol

Introduction

Physical stress activates the sympathetic-adrenal-medullary (SAM) and hypothalamic-pituitary-adrenocortical (HPA) axes. The sympathetic nervous system response of the SAM axis is instantaneous and results in the release of norepinephrine from sympathetic neurons.¹ In contrast, the release of the catecholamines epinephrine (80%) and norepinephrine (20%) from the adrenal medulla may take minutes to hours.¹ The HPA axis stimulates corticotropin-releasing hormone (CRH) release from the hypothalamus, adrenocorticotrophic hormone (ACTH) from the anterior pituitary, and cortisol from the adrenal cortex.²

Exercise activates both the SAM and HPA axes. Levels of norepinephrine and epinephrine increase during exercise³ proportional to changes in exercise intensity.⁴ Cortisol is released during both short-duration high-intensity exercise and long-duration low-intensity exercise.² The combined effects of these stress hormones include enhanced responsiveness of the cardiovascular system and fuel mobilization. Although much is understood about the physiologic responses to endurance events lasting 1 to 3 hours, far less is known about ultraendurance events lasting more than 4 hours. During ultraendurance exercise, norepinephrine and epinephrine have been reported to increase^{5–8} or not change.^{6,7} Adrenocorticotrophic hormone has been found to not change,^{5,6,9} and cortisol typically increases.^{5–14}

Environmental stress also activates the SAM and HPA axes as the body attempts to maintain a thermoneutral

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Table 1. Descriptive characteristics of subjects

Division, gender	2003 (n)	2004 (n)	Total (n)
Foot, male	8	8	16
Foot, female	3	1	4
Bike, male	4	10	14
Bike, female	0	3	3
Ski, male	0	6	6
Ski, female	0	1	1

internal environment. Although much research has been done on heat stress, far less is known about the body's response to a cold environment. During resting cold exposure, increases in norepinephrine, epinephrine, ACTH, and cortisol result in heat production, fuel mobilization, and decreased heat loss.^{15,16} During exercise in the cold, norepinephrine and epinephrine have been reported to increase^{17–21} or not change.^{18,22,23} Adrenocorticotrophic hormone has been found to not change,²⁴ and cortisol may increase,^{24–26} decrease,²⁷ or not change.^{21,28}

The combination of ultraendurance exercise in the cold presents a unique summated stress to the body. The purpose of the current study was to examine the stress hormone response in athletes participating in the Susitna 100. This event is a 160-km human-powered ultramarathon held in the Alaskan wilderness each February. Athletes compete on the same snow-packed course in one of three divisions: foot, bike, or ski. This race provides a novel opportunity to evaluate how stress hormones respond to an extreme exercise and environmental stress.

Materials and methods

All 138 entrants in the 2003 and 2004 Susitna 100 were invited to participate in the study at the mandatory informational meeting held 2 days before the start of the race. In total, 44 athletes (Table 1) volunteered to be subjects and signed a written informed consent document approved by the Gettysburg College institution review board. The small sample size of some of the groups (eg, female skiers) was a limitation of this study. No training or acclimatization data were collected.

The athletes in each of three divisions (foot, bike, and ski) competed on the same 161-km (100-mile) snow-packed course that wound through the Alaskan wilderness and included an elevation gain of 2270 m. Approximately 132 km (82 miles) of the course were snow-machine trails, and the remaining 29 km (18 miles) were ice roads on frozen lakes and rivers. Five checkpoints were located approximately every 24 to 32 km (15 to 20 miles), where food and fluid were available. Ath-

letes were required to carry 7 kg (15 pounds) of mandatory equipment at all times, including a sleeping bag and pad, a tent, a stove, fire starter, fuel and pot, a headlamp, 2 L of fluid in an insulated container, and 3000 kcal of food. Runners typically wore neoprene socks with running shoes and carried their gear on a sled. Cyclists rode mountain bikes with the widest rims and fattest tires that would fit on their bikes. They carried their gear in backpacks and strapped to their bikes. Skiers typically competed on skate skis and carried their gear in backpacks.

In 2003, temperatures during the race ranged from -9°C to -4°C (16°F to 25°F) with an average wind speed of 3 km/h (2 mph). Average humidity was 82%, and there was no precipitation. Temperatures ranged from -11°C to -2°C (11°F to 31°F) with an average wind speed of 0.5 km/h (0.3 mph) in 2004. Average humidity was 85%, and very light snow fell during the beginning of the race.

The timing of prerace and postrace measurements was a limitation of this study. Due to the nature of the race, it was not possible to collect prerace measurements immediately prior to the race start. All prerace measurements were made 2 days before the race at approximately 6:00 PM at a mandatory informational meeting. Postrace measurements were made within 15 minutes of each athlete completing the race, with the time of day varying based on finish time. The gap between prerace measurements and the race start limited interpretation of prerace and postrace data. The varied time of day for postrace measurements limited interpretation of ACTH and cortisol results, as these hormones are released according to an in vivo circadian rhythm, with a morning maximum and a nocturnal nadir.²⁹

Prerace and postrace weights were measured using the Tanita Body Fat Monitor/Scale (TBF-622; Arlington Heights, IL), accurate to ± 0.1 kg. Prerace and postrace blood samples were collected by routine venipuncture with athletes in a sitting position. Hematocrit was measured using standard procedures at the Alaska Regional Hospital in Anchorage, Alaska. Percentage change in plasma volume was calculated according to the formula of van Beaumont³⁰: % change plasma volume = $(100/100 - \text{hematocrit}_{\text{pre}}) \times 100 (\text{hematocrit}_{\text{pre}} - \text{hematocrit}_{\text{post}})/\text{hematocrit}_{\text{post}}$, where $\text{hematocrit}_{\text{pre}}$ and $\text{hematocrit}_{\text{post}}$ are prerace and postrace hematocrit samples, respectively. Stress hormones were measured from ethylenediamine tetraacetic acid (EDTA)-anticoagulated plasma that was obtained by centrifugation in Vacutainer tubes, frozen immediately on dry ice, and stored at -20°C until thawed for analysis. Norepinephrine and epinephrine were measured at Walter Reed Army Research Institute (Washington, DC). Catecholamine isolation was

Table 2. Physical characteristics of subjects (values expressed as mean $\pm$ SD)

	<i>Runners</i> (<i>n</i> = 20)	<i>Cyclists</i> (<i>n</i> = 17)	<i>Skiers</i> (<i>n</i> = 7)	<i>Total</i> (<i>n</i> = 44)
Age (y)	45 $\pm$ 11	34 $\pm$ 15	37 $\pm$ 9	39 $\pm$ 13
Height (cm)	177 $\pm$ 9	177 $\pm$ 7	180 $\pm$ 9	178 $\pm$ 8
Prerace body mass (kg)	79.3 $\pm$ 12.4	78.7 $\pm$ 10.8	78.9 $\pm$ 5.0	79.0 $\pm$ 10.7
Postrace body mass (kg)	77.5 $\pm$ 12.5 ^a	78.1 $\pm$ 10.8	78.9 $\pm$ 4.4	78.0 $\pm$ 10.7 ^a
Δ body mass (kg)	-1.74 $\pm$ 1.29	-0.64 $\pm$ 1.37	0.0 $\pm$ 1.46	-1.04 $\pm$ 1.48
Percentage Δ body mass (%)	-2.25 $\pm$ 1.65	-0.79 $\pm$ 1.78	0.0 $\pm$ 1.87	-1.32 $\pm$ 1.92
Finish time (h)	33.3 $\pm$ 6.1	24.9 $\pm$ 5.4	22.4 $\pm$ 6.0	28.3 $\pm$ 7.4

^a $P < .05$ postrace vs prerace body mass.

accomplished by alumina extraction using a Chrom-systems reagent kit (Chromsystems; Munich, Germany). Once extracted, plasma catecholamine concentration was quantified by high-pressure liquid chromatography (HPLC) using a complete Waters system (Milford, MA). Using this system, the between-days coefficient of variation is less than 3%, the within-days variation is less than 1%, the coefficient of correlation from 5 to 1000 pg is 0.9980, and sensitivity is 5 pg with a signal-to-noise ratio of 12 to 1. Adrenocorticotrophic hormone and cortisol concentrations were measured at the United States Army Research Institute of Environmental Medicine (Natick, MA) by enzyme-linked immunoabsorbent assays (Diagnostic Systems Laboratories, Webster, TX). All samples were performed within one assay batch to eliminate interassay variance. Intra-assay variances were $<7\%$.

Two (year or sex) $\times$ 2 (trial) between-within factorial analyses of variance evaluated if any significant changes between prerace and postrace body mass and blood measures differed by race year or sex. A 3 (division) $\times$ 2 (trial) between-within factorial analysis of variance evaluated if any significant changes between prerace and postrace body mass and blood measures differed by division. Follow-up analyses included simple ANOVA and paired t tests, as appropriate. Data were analyzed using StatView software (SAS Institute Inc., Cary, NC) with statistical significance set at $P \leq .05$.

Results

Changes in prerace and postrace weight and blood measures did not differ significantly by race year or sex, so the 2003/2004 and male/female data were combined for subsequent analyses. Table 2 presents physical characteristics and race results for subjects split by division. Prerace and postrace blood measurements by division are shown in Table 3.

Subjects lost significant ($P = .001$) weight prerace to postrace ($-1.04 \text{ kg} \pm 1.48$) with differences by division ($P = .007$). Follow-up paired t tests split by division indicated a significant ($P < .0001$) decrease in weight for the runners ($-1.74 \text{ kg} \pm 1.29$) with no significant change for the cyclists ($-0.64 \text{ kg} \pm 1.37$) or skiers ($0.00 \text{ kg} \pm 1.46$).

Hematocrit did not change significantly prerace to postrace, and plasma volume increased minimally ($2.4\% \pm 8.0$). Norepinephrine increased significantly ($P < .0001$) prerace ($279.9 \text{ pg/mL} \pm 356.9$) to postrace ($691.7 \text{ pg/mL} \pm 422.6$) with no difference among divisions. Epinephrine did not change significantly during the race. There was a significant ($P = .02$) increase in ACTH prerace ($2.40 \text{ pg/mL} \pm 2.40$) to postrace ($19.04 \text{ pg/mL} \pm 45.38$) with no difference among divisions. Cortisol increased significantly ($P < .0001$) prerace ($12.03 \text{ } \mu\text{g/dL} \pm 5.66$) to postrace ($26.69 \text{ } \mu\text{g/dL} \pm 5.77$) with differences by division ($P = .0410$). Follow-up paired t tests split by division indicated a significant increase in cortisol prerace to postrace for the runners ($P < .0001$), cyclists ($P < .0001$), and skiers ($P < .0001$). Follow-up simple ANOVA across divisions revealed significantly higher cortisol levels postrace for the runners compared with those of the skiers ($P = .02$).

Discussion

Compared with endurance exercise or heat stress, little research has been done on ultraendurance exercise or cold stress. Even less is known about ultraendurance exercise performed in a cold environment. This study evaluated prerace and postrace levels of the stress hormones norepinephrine, epinephrine, ACTH, and cortisol in runners, cyclists, and skiers competing in the Susitna 100, an ultraendurance race held on a snow-packed trail in the Alaskan wilderness each February.

Table 3. Blood measures (values expressed as mean $\pm$ SD)

	Runners (<i>n</i> = 20)	Cyclists (<i>n</i> = 17)	Skiers (<i>n</i> = 7)	Total (<i>n</i> = 44)
Norepinephrine (pg/mL)				
Prerace	253.3 $\pm$ 409.9	320.5 $\pm$ 369.5	257.6 $\pm$ 93.8	279.9 $\pm$ 356.9
Postrace	664.4 $\pm$ 403.6	631.6 $\pm$ 476.0	915.3 $\pm$ 297.8	691.7 $\pm$ 422.6 ^a
Epinephrine (pg/mL)				
Prerace	21.6 $\pm$ 12.9	36.7 $\pm$ 23.1	35.9 $\pm$ 16.0	29.7 $\pm$ 19.1
Postrace	45.6 $\pm$ 44.8	69.6 $\pm$ 151.2	66.5 $\pm$ 90.1	58.2 $\pm$ 103.8
ACTH (pg/mL)				
Prerace	2.20 $\pm$ 1.66	1.56 $\pm$ 0.74	5.04 $\pm$ 4.56	2.40 $\pm$ 2.40
Postrace	28.73 $\pm$ 61.93	6.80 $\pm$ 10.34	21.11 $\pm$ 39.79	19.04 $\pm$ 45.38 ^a
Cortisol (μ g/dL)				
Prerace	12.17 $\pm$ 5.76	11.28 $\pm$ 6.32	13.50 $\pm$ 3.73	12.03 $\pm$ 5.66
Postrace	28.85 $\pm$ 4.11 ^{ab}	25.74 $\pm$ 6.75 ^a	22.85 $\pm$ 5.35 ^a	26.69 $\pm$ 5.77 ^a
Hematocrit				
Prerace	40.9 $\pm$ 3.8	42.0 $\pm$ 2.7	41.6 $\pm$ 2.9	41.3 $\pm$ 3.3
Postrace	40.6 $\pm$ 3.8	41.9 $\pm$ 2.5	39.4 $\pm$ 1.4	40.9 $\pm$ 3.2
Percentage Δ plasma volume (%)	1.6 $\pm$ 8.6	0.7 $\pm$ 5.6	9.6 $\pm$ 8.5	2.4 $\pm$ 8.0

^a *P* < .05 prerace vs postrace norepinephrine, ACTH, or cortisol.^b *P* < .05 runners vs skiers postrace cortisol.

Plasma norepinephrine is used as an acute marker of sympathetic nervous system activity as norepinephrine is released from peripheral sympathetic nerve endings during stress.¹⁶ Not surprisingly, norepinephrine increased significantly in the current study, indicating activation of the SAM axis during an ultraendurance race in the cold. This finding is similar to the results of Dulac et al,⁸ who reported increased norepinephrine levels after a 9-hour cold-water swim. Our results also are consistent with the results of temperate ultraendurance races. Increased norepinephrine was reported after a 24-hour run,⁷ a 7-day road race,⁶ and a triathlon.⁵

The response of epinephrine to ultraendurance exercise is variable. Dulac et al⁸ reported increased epinephrine levels after a 9-hour cold-water swim, and epinephrine increased after a temperate triathlon.⁵ In contrast, epinephrine levels did not change after a 7-day footrace,⁶ a 24-hour run,⁷ a triathlon,⁷ or in the current study. Exercise cold-stress studies suggest that epinephrine responds to changes in core body temperature. When core body temperature decreased during exercise-cold stress, epinephrine increased.^{19–21} In contrast, when core body temperature was maintained during exercise in a cold environment, epinephrine either did not change or decreased.^{19,23} Core body temperature was not measured in the current study. However, the rugged, unpredictable nature of the Susitna 100 course typically results in athletes completing the race by maintaining a slow, steady pace, as indicated by the finish times. By constantly moving, it is possible that the athletes were able

to maintain their core body temperature despite the cold environment and that an epinephrine response was not elicited.

Both exercise and psychological stress elicit a catecholamine response.³¹ However, it has been suggested that the sympathetic nervous system responds to exercise, causing elevated norepinephrine levels, and that the adrenal medulla responds to psychological stress, resulting in increased levels of epinephrine.³² Consistent with this idea, increased norepinephrine levels in the current study could be attributed to exercise. Although there were many potential psychological stressors in this race (sleep deprivation, apprehension about getting lost, concern over running out of food/fluid, fear of encountering wildlife), the lack of an epinephrine response may indicate that the athletes were able to manage the psychological stress of the event. Alternatively, adaptation to the continual psychological stress of the race may have occurred, similar to the adaptation that occurs after repeated exposure to the same stimulus.³³

The significant increase in ACTH and cortisol prerace to postrace in this study indicated activation of the HPA axis. Prerace cortisol levels (12.03 μ g/dL $\pm$ 5.66) were within the normal range (5 to 23 μ g/dL)³⁴ but the post-race levels (26.69 μ g/dL $\pm$ 5.77) were outside the normal range, suggesting the severe stress this race imposed on athletes. The cortisol response during the Susitna 100 is consistent with that of other ultraendurance events in the cold. Cortisol increased during a 75-km ski race¹⁴ and after a 32-km swim in 18.5°C water.⁸ The cortisol

results in this study also are similar to those of ultraendurance events in mild temperatures. Studies consistently find increased cortisol levels after prolonged exercise.^{5-7,9-11,13} The results of this and other studies clearly indicate that cortisol secretion increases in response to exercise and cold stresses. However, additional stresses besides exercise and cold possibly contributed to the increased cortisol levels observed in the current study. Decreased blood glucose levels increase blood cortisol levels,^{35,36} as does acute weight loss.³⁷ The athletes in the current study lost significant weight prerace to postrace ($-1.04 \text{ kg} \pm 1.48$), and their blood glucose levels likely were decreased. Corticotropin-releasing hormone is the primary stimulus for the secretion of ACTH and cortisol in the HPA axis,² but arginine vasopressin (AVP) also can cause a similar response.³⁸ Both osmotic and non-osmotic stimuli increase AVP secretion during endurance exercise,³⁹ possibly contributing to the increased cortisol levels in the current study. Finally, the athletes in the Susitna 100 were sleep deprived during the race (finish time $28.3 \text{ h} \pm 7.4$), and it has been reported that loss of sleep stimulates cortisol release.⁴⁰

The cortisol response differed by division in the current study. Cortisol increased significantly in all three groups prerace to postrace (Table 3), but the runners had significantly higher postrace cortisol levels ($28.85 \text{ } \mu\text{g/dL} \pm 4.11$) compared with those of the skiers ($22.85 \text{ } \mu\text{g/dL} \pm 5.35$). The runners were slower, finishing the race in 33.3 hours compared with 22.4 hours for the skiers. Furthermore, the runners lost significant weight during the race (-2.25%) compared with the skiers, who maintained their weight. The increased cortisol response in the runners likely was caused by the increased duration of exercise and the significant weight loss.

In summary, the findings of this study provide specific information on the stress hormone response in athletes undergoing the unique summated stress of ultraendurance exercise in the extreme cold. Although it is difficult to determine if changes in stress hormones are attributed to ultraendurance exercise, extreme cold, or a combination of both, our data indicate activation of the SAM and HPA axes during this unique event.

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