Adrenal Stress and Physical Performance During Military Survival Training

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INTRODUCTION: The purpose of this research was to evaluate neuroendocrine and physical performance responses in sailors and Marines undergoing U.S. Navy Survival, Evasion, Resistance, and Escape (SERE) training.

METHODS: Participants were 20 men (Age: 25.3 ± 3.6 yr; Height: 178.1 ± 6.1 cm; Weight: 83.7 ± 12.6 kg). Men were further split into high fit ($N = 10$) and low fit ($N = 10$) subgroups based on physical fitness test scores. Blood samples were obtained at baseline (T1), stress (T2), and recovery (T3) timepoints, and were analyzed for plasma epinephrine, plasma norepinephrine, plasma dopamine, serum cortisol, serum testosterone, and plasma neuropeptide Y. Vertical jump and handgrip tests were performed at T1 and T2.

RESULTS: Stress hormone concentrations were significantly elevated at T2, with a concomitant reduction in testosterone concentrations. NPY concentrations did not increase at T2, but decreased significantly at T3. Subjects maintained performance on vertical jump and handgrip tests from T1 to T2. Significant between group differences were observed in norepinephrine (high fit: 3530.64 ± 2146.54 pmol · L^{-1}, low fit: 4907.16 ± 3020.85 pmol · L^{-1}) and NPY (high fit: 169.30 ± 85.89 pg · ml^{-1}, low fit: 123.02 ± 88.86 pg · ml^{-1}) concentrations at T3.

CONCLUSION: This study revealed that despite significant increases in stress hormone concentrations in all subjects during SERE, fitter subjects exhibited differential hormonal responses during recovery, with quicker return of norepinephrine and NPY to baseline concentrations. This suggests physical fitness level may have a protective effect in recovery from periods of high stress military training.

KEYWORDS: SERE, endocrine, cortical, neuromuscular, adreno-medullary.

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Over the course of a military career, soldiers are exposed to many different stressors, ranging from environmental extremes (e.g., heat or cold exposure), to physical demands (e.g., load carriage), to psychological or operational demands. Challenging operational and training requirements can push the limits of existing performance capabilities or exceed one's ability to adapt to additional stressors. Fatigue, sleep deprivation, inadequate nutrition, and suboptimal recovery strategies combined with taxing mission requirements can ultimately overwhelm the body's ability to respond to a given magnitude of stress.[11,25] Thus, how well soldiers are able to tolerate operational and training demands and respond to these stressors over time has an impact on long-term resilience and health.

One of the factors that influences how well an individual tolerates stress is level of physical fitness, specifically, neuromuscular performance. Not only that, studies have shown that fitness level offers protection against the negative effects of stress, and can have positive impacts on health, disease hardiness, and immune function.[29,36] Additionally, one's level of fitness can impact the extent to which one is able to adapt to stressors of varying nature in both a training and operational setting and is thus an important consideration in terms of mission readiness. For these reasons, maintaining optimal physical fitness as part of an overall resiliency strategy is of utmost importance for the health and longevity of the soldier over the course of a military

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career. Research regarding the differences in stress response among soldiers of varying fitness levels can inform command decisions about structuring strenuous military training in ways that minimize negative effects on recovery and resilience, while still meeting training objectives and enhancing mission readiness.

To best understand the magnitude of stress soldiers may experience both in a training environment and operationally, and to put the value of physical fitness in context, it is helpful to study the effects of strenuous military training in as realistic of a setting as possible. One such course is the United States Navy Survival, Evasion, Resistance, and Escape (SERE) course, hereafter referred to as SERE. Although portions of the SERE course content are classified, the general purpose of SERE is to teach trainees how to survive in austere environments, how to evade capture by the enemy, how to resist exploitation and survive if captured, and ultimately how to escape capture. The course is designed to be highly realistic, and culminates with an intense captivity experience modeled after the experiences of prisoners of war (POWs) that has been described elsewhere.[21] SERE exposes trainees to a multitude of stressors which may be faced in a survival or captivity situation: environmental extremes (i.e., heat or cold exposure), physical demands, food deprivation, sleep deprivation, and psychological stress.[22,31,32] Thus, the SERE course offers an ideal avenue to measure physiological stress responses in a highly stressful training environment and is a unique opportunity for study.

"Stress" is defined as the body's adaptation to a specific demand.[28] As the human body constantly strives for homeostasis, stress can be further defined as any type of perturbation in the physiological system (i.e., an internal or external demand) that causes a shift away from homeostasis and requires alterations in physiological processes in order for the body to respond to the given demand and eventually return to a homeostatic state. Although the sources of stress can be varied (i.e., mental vs. physical stressors), the physiological response to stress is much the same, involving activation of the adrenal system and the associated hormonal cascades. The stress response is characterized by activation of the hypothalamic-pituitary-adrenal (HPA) axis and increased glucocorticoid secretion from the adrenal cortex, along with coactivation of the sympathetic nervous system (SNS), resulting in increased catecholamine release from the adrenal medulla, often termed the "fight or flight" response.[26,28] While these are normal physiological responses to stress, it is worth noting that either the lack of a response to a stressor or a hyperactive response beyond normal physiological ranges can be a concern for optimal physiological regulation of the body's homeostatic mechanisms for survival.

In order to assess the effects of a high-stress training environment such as SERE and evaluate associations between fitness level and stress responses, several neuroendocrine hormones are of interest: specifically, biomarkers of adrenergic stress (i.e., the catecholamines dopamine, epinephrine, and norepinephrine), biomarkers of adreno-cortical stress (cortisol and testosterone), and the neurotransmitter neuropeptide Y (NPY).

Under adrenergic arousal, catecholamines are released within seconds as a rapid response to stress, with epinephrine as the predominant secretion. This release occurs upon sympathetic nervous system activation with exocytosis and fusion with the glandular membrane or alternatively with generalized degranulation and release directly into circulation.[7,26] While catecholamine release is rapid in response to stress it is also rapid in return to normal resting concentrations once the sympathetic drive is reduced. However, alternative pathways (i.e., piecemeal degranulation) may give rise to chronic increases in catecholamines beyond sympathetic innervation.[7] Therefore, catecholamine elevations at rest (i.e., in the absence of exercise) are indicative of a dramatic stress condition that potentially represents a maladaptive physiological environment (i.e., perturbation from homeostasis).

Whereas catecholamine response is immediate, cortisol must be synthesized and released into circulation. The rate of cortisol synthesis determines the quanta of hormone released.[26] Basal cortisol concentrations are indicative of the level of adrenal stress the body is operating under physiologically, and when significantly elevated can represent a catabolic hormonal milieu.[24] Thus, resting cortisol values leading into any operational environment or high-stress training scenario set the stage for the soldier's ability to respond to additional stressors and give context to understanding cortisol elevations that occur in the absence of physical exercise. Importantly, the inability of the adrenal gland to respond effectively to a stressful situation has implications as to one's mission readiness and resilience. Conversely, a hyper-responsivity of the adrenal cortex can reflect an uncontrolled dysregulation in response to a given stressor.

In the context of stressful military training, it is helpful to view elevations in cortisol in relation to testosterone concentrations. Strenuous military training courses involving increased energy expenditure, caloric deficit and sleep deprivation have been shown to negatively affect resting testosterone concentrations in men.[18,21,24] Heavy physical demands and frequent endurance exercise can result in lower resting concentrations of testosterone, often as a function of increased testosterone uptake at the steroid receptor level.[12] Thus, lower resting testosterone concentrations in an active male population do not necessarily indicate hypogonadism, but more often reflect physical activity status. Therefore, resting testosterone concentrations in men at the onset of military training courses can provide context and understanding related to one's anabolic status, particularly when viewed with associated cortisol elevations, and can aid in the interpretation of training-induced testosterone changes.

Finally, NPY, a 36-amino acid neurotransmitter, has been implicated in the stress response as it is involved with regulation of the noradrenergic system both centrally and in the periphery.[22,23] Although the various functions of NPY in the body remain to be fully elucidated, reductions in NPY are thought to relate to maladaptive stress responses, whereas increased NPY levels may be a key factor in improved stress tolerance.[20,22,23] Previous research has attributed differences in NPY response to level of training, while other studies have

associated elevated NPY with resilience to posttraumatic stress disorder (PTSD).[22,27,30] Of interest to the present research, elevations in NPY have been correlated with increased cortisol and norepinephrine concentrations during periods of "uncontrollable stress" in previous SERE investigations.[22,23] Thus, NPY concentrations can provide context for the interpretation of adrenal stress responses during SERE training.

To date, limited research has been done to evaluate the relationship between physical fitness level and associated hormonal stress responses during SERE, and virtually no data have been published on physical performance during U.S. SERE training. Existing SERE investigations have focused largely on psychological, cognitive, and neuroendocrine factors.[18,22,34] One SERE investigation attributed magnitude of hormonal stress response during "uncontrollable stress" to level of training (as measured by physical fitness test scores).[31] In terms of physical performance, evaluation of upper body strength and global body power and any associated performance alterations over the course of SERE provides useful context for interpretation of training stresses when viewed in concert with neuroendocrine responses. Because the SERE training environment is restricted, field-expedient measures of physical performance such as handgrip and vertical jump testing can provide valuable performance data without compromising the integrity of the SERE training course.

The present investigation offers a unique opportunity to expand upon prior work in the SERE population and further explore relationships among fitness level, physical performance and neuroendocrine responses. Thus, the purpose of this investigation was threefold: 1) to examine the effects of SERE on neuroendocrine responses; 2) to examine the effects of SERE on physical performance measures; and 3) to assess differences in neuroendocrine responses or physical performances due to physical fitness level. We hypothesized that individuals of higher physical fitness level would have improved recovery from the effects of SERE stress, as evidenced by quicker return of stress hormone concentrations to baseline values.

METHODS

Subjects

This field study represented a rare opportunity to study the physiological stresses associated with Navy SERE training, which was conducted over a 2-wk period in Kittery and Rangeley, ME, during March 2016. Study participants ($N = 20$) were active duty men serving in the U.S. Navy and Marine Corps. Four women also participated in the research study; however, their data are not included in the statistical analysis due to insufficient n-size. The men ranged in age from 18 to 35 yr old and had been serving at their respective duty locations prior to arrival at SERE. Subjects were asked to complete a physical activity questionnaire as part of their baseline assessment. Additionally, self-reported physical fitness test scores were obtained from each subject. Navy sailors reported their most recent Physical Readiness Test (PRT) scores, while Marines reported their most recent Physical Fitness Test scores (PFT). Each subject provided written informed consent before participating, which included information regarding the subject's option to withdraw from the study at any time during the SERE training course. The study protocol was approved by The Ohio State University's Institutional Review Board (IRB) for use of human subjects in research. The Ohio State University IRB served as the IRB of record for Department of Defense (DoD)-Department of the Navy (DON) research under the DoD-DON Addendum to the Department of Health and Human Service's Federalwide Assurance (FWA) for the Protection of Human Subjects. **Table I** presents the relevant participant characteristics.

Table I. Participant Characteristics.*

	HIGH FIT GROUP ($N = 10$ MEN)	LOW FIT GROUP ($N = 10$ MEN)	WOMEN ($N = 4$) †
Age (years)	25.30 (± 4.39)	25.20 (± 9.02)	22.25 (± 2.49)
Height (cm)	176.22 (± 10.81)	180.00 (± 12.24)	163.88 (± 4.09)
Weight (kg)	82.21 (± 17.85)	85.24 (± 30.40)	67.19 (± 5.11)
Physical fitness score (total points)	265.30 (± 28.17)	207.50 (± 58.69)‡	251.20 (± 28.44)
Baseline (T1) vertical jump (cm)	59.06 (± 32.62)	54.36 (± 22.46)	39.37 (± 6.78)
Baseline (T1) dominant handgrip (kg)	53.40 (± 17.13)	46.65 (± 15.12) ‡	33.50 (± 3.20)
Workouts per week (self-report)	5 or more ($N = 1$)	3 to 5 ($N = 5$)	5 or more ($N = 1$)
	3 to 5 ($N = 8$)	Less than 3 ($N = 4$)	3 to 5 ($N = 2$)
	Less than 3 ($N = 1$)	No answer ($N = 1$)	Less than 3 ($N = 1$)
Self-assessed fitness level	Excellent ($N = 1$)	Very Good ($N = 4$)	Very Good ($N = 2$)
	Very Good ($N = 8$)	Good ($N = 4$)	Good ($N = 2$)
	Fair ($N = 1$)	Fair ($N = 1$)	
		No answer ($N = 1$)	
Military experience (months)	57.10 (± 86.65)	50.30 (± 64.65)	36.50 (± 28.58)
Deployed experience	($N = 3$)	($N = 3$)	($N = 1$)

* Relevant subject characteristics. Physical fitness score: For Navy sailors, Physical Readiness Test (PRT) scores were used. For Marines, Physical Fitness Test (PFT) scores were used. The PRT (Navy) is a three-event test consisting of the maximum number of pushups performed in 2 min, the maximum number of sit-ups performed in 2 min, and a 1.5 mile timed run. The PFT (Marines) consists of the maximum number of pullups in 2 min, the maximum number of sit-ups in 2 min, and a 3-mile timed run. Physical activity scale: Less than 3 times per week, 3 to 5 times per week, or 5 or more times per week. Self-assessed fitness level: Poor, fair, good, very good, or excellent. Deployed experience: One or more deployment to a combat or hostile zone.

† Women's data were not included in statistical analysis. Data are presented as mean (± SD).

‡ Significant differences from the high fit group ($P \leq 0.05$).

Design

The Navy SERE course is approximately 2 wk in duration, beginning with a 4-d didactic phase, followed by an experiential (field) training phase (evasion and capture). Three testing timepoints were used to examine the different temporal progressions of the course: a baseline assessment (T1), which occurred on the first day of SERE training; a stress assessment (T2), which occurred 10 d after T1; and a recovery assessment (T3), which occurred 24 h after T2. Subjects were recruited, consented to participation, and were familiarized with study procedures on the baseline test day (T1). We obtained blood samples at all three testing time points and collected physical performance data (handgrip test and vertical jump) at two testing time points (T1 and T2). All testing for this study occurred between the hours of 1800 and 2200.

Equipment

We selected field-expedient physical performance measures for this investigation due to command restrictions and our desire to maintain the integrity of the SERE plan of instruction. The handgrip test for grip strength was used as an analytical measure of global body strength and was performed using an analog handgrip dynamometer (Takei model 5001, Takei Scientific Instruments Co., LTD, Niigata, Japan). Subjects were instructed to grip the handgrip dynamometer in the dominant hand, and squeeze as hard as possible for approximately 5 s. The test was then repeated on the nondominant hand. Three attempts were performed for each test and the highest recorded values were used for subsequent analysis. The vertical jump test was used as an analytical measure of maximal lower body power output and was conducted using a Vertec testing device (JumpUSA, Sunnyvale, CA). Subjects completed the vertical jump wearing a military-issued field uniform without footwear to control for variance in footwear from one testing visit to another. Participants were asked to jump as high as they could using a countermovement technique, extending their dominant arm overhead and reaching as high as possible on the Vertec device. Three attempts were performed for each test and the highest value was used for subsequent analysis.

Procedures

The baseline assessment (T1) occurred on the first day of SERE training; anthropometric data, baseline blood samples, and baseline neuromuscular performance data were obtained. Body mass was recorded for each subject, after which a resting blood sample was obtained. After blood draws had been completed, subjects then performed the handgrip test followed by the vertical jump assessment. Prior to any baseline testing, study procedures were described in detail and subjects were familiarized with each of the performance tests to be used in the study. On this day, subjects ate a lunch of their choice at approximately 1200 h and were asked to provide a dietary record of this meal.

At the conclusion of the didactic portion of the SERE course, trainees then began the experiential portion of SERE training (evasion and capture phases). During the evasion phase, subjects underwent several days of field training during which they practiced evasion techniques and were required to traverse several miles of steep snow-covered terrain while carrying a military-issue rucksack, in addition to several layers of cold weather gear. The subsequent capture phase culminated in several high-stress training scenarios designed to provide trainees with a realistic captivity experience leading up to the stress assessment (T2). Due to the classified nature of certain aspects of SERE training, an exact description of this training phase is not possible; however, it has been described elsewhere and includes several interrogations, solitary confinement, and problem solving dilemmas.[21]

The timing of the stress assessment (T2) was governed by the SERE course schedule, and occurred after two interrogation sessions separated by a period of solitary confinement, a timepoint which the SERE instructors had assessed as the most stressful portion of the training course. Leading up to this timepoint (T2), subjects had been subjected to several days of food restriction and sleep deprivation, while contending with physical demands, environmental stressors (i.e., cold exposure) and psychological stressors (i.e., interrogations and solitary confinement). Immediately after the period of solitary confinement and the second interrogation, trainees were brought into a room at the training compound where body mass was recorded and blood draws were obtained. After blood draws, subjects were given a high-carbohydrate snack and allowed to rest for approximately 5 min. This was done at the command's request to mitigate any potential negative effects following the blood draw due to the subjects' fasted state at this point in the training course. Following the rest period, subjects then performed the handgrip test and the vertical jump test.

The recovery assessment (T3) occurred on the final day of SERE training, 24 h after the stress assessment. At this timepoint, we again recorded the subject's body mass and obtained a resting blood sample; however, no performance tests were conducted. Prior to the recovery assessment, at approximately 1200 h, subjects were provided with a bag lunch consisting of a sandwich, chips, fruit and water. Subjects were asked to provide a record of what they had eaten at this meal.

Biochemical Analyses

Blood samples were obtained via a 20-gauge needle and syringe with butterfly clamp and vacutainers. Trained phlebotomists performed all blood draws using standard phlebotomy procedures. Subjects were seated and allowed to rest quietly for approximately 5 min prior to each draw. On each test day, approximately 40 ml of blood were collected into sample tubes specific for each type of analyte. As this was a field study, blood processing occurred on-site. Collected blood samples were immediately centrifuged at 3000 rpm for 15 min at 4°C. After centrifugation, resulting serum or plasma was spun, aliquoted, and immediately placed on dry ice on-site for subsequent shipment to the processing analytical laboratory. These procedures were followed in the same manner for all three testing timepoints to minimize any variation in the data due to specimen handling techniques. Serum cortisol, serum testosterone and plasma neuropeptide Y were analyzed via Direct

Radioimmunoassay (Quest Diagnostics, Wood Dale, IL). Plasma catecholamines (epinephrine, norepinephrine, and dopamine) were determined via High Performance Liquid Chromatography (HPLC) (Quest Diagnostics, Wood Dale, IL). No genetic testing was performed for this study. Measures were performed in duplicate with intra- and interassay differences typically under 5 and 10%, respectively.

Statistical Analyses

The data from this investigation were analyzed using a 1 × 3 group ($N = 20$) by time linear model one-way analysis of covariance with repeated measures. Physical fitness level (based on physical fitness test score) was used as the covariate of interest. Where significant differences were observed, a post hoc analysis of pairwise comparisons was conducted, using a Fishers LSD post hoc test. A subsequent two-group analysis of variance was performed, splitting subjects into high fit ($N = 10$) and low fit ($N = 10$) subgroups based on military physical fitness test scores. Independent *t*-tests were used to calculate differences between groups at each timepoint. Data were analyzed for the assumptions of linear statistics and if the data set did not meet the assumptions a log10 transformation was used. A Pearson product-moment correlation matrix was used to determine associations among the experimental variables at each test day. Statistical significance for this investigation was set at $P \leq 0.05$. The data are presented as means ± SD.

RESULTS

As shown in **Table II**, exposure to SERE stress resulted in significant increases in plasma epinephrine, plasma norepinephrine, plasma dopamine and serum cortisol concentrations, with a concomitant reduction in serum testosterone concentrations in men. No significant elevations in plasma NPY were observed at T2; however, a significant reduction in NPY was observed at T3.

As shown in Table II, exposure to SERE stress did not result in significant differences in handgrip or vertical jump scores from T1 to T2 in men. However, we observed significant reductions in body mass from baseline at T2 and T3.

For plasma norepinephrine, analysis of covariance demonstrated that physical fitness level influenced the magnitude of change in distributions over the three test days ($F(1,18) = 4.43$, $P = 0.05$). Subsequent between group analyses showed significantly lower norepinephrine values ($P = 0.03$) in the high fit group at T3. Mean differences in norepinephrine concentrations ($pmol \cdot L^{-1}$) between the high fit and low fit groups are presented in **Fig. 1**.

For plasma neuropeptide Y, although covariate analysis did not detect the influence of physical fitness level on the pattern of change over the 3 test days ($F(1,18) = 0.06$, $P = 0.81$), subsequent between group analyses showed significantly higher NPY values ($P = 0.03$) in the high fit group at T3. Mean differences in NPY concentrations ($pg \cdot ml^{-1}$) between the high fit and low fit groups are presented in **Fig. 2**.

Physical fitness level did not influence the magnitude of change in plasma epinephrine ($F(1,18) = 0.39$, $P = 0.54$), plasma dopamine ($F(1,18) = 0.13$, $P = 0.72$), serum cortisol ($F(1,18) = 0.07$, $P = 0.80$) or serum testosterone ($F(1,18) = 0.77$, $P = 0.39$) concentrations in men across testing timepoints.

For the dominant hand, covariate analysis detected that physical fitness level influenced the changes in the mean distributions of handgrip scores over the testing time points ($F(1,18) = 5.29$, $P = 0.03$). Subsequent between group analyses revealed significantly higher handgrip scores in the high fit group at baseline (T1). However, physical fitness level did not influence the magnitude of change in vertical jump performance ($F(1,18) = 1.57$, $P = 0.23$) or changes in body mass ($F(1,18) = 0.04$, $P = 0.85$) across testing timepoints.

Although women's data were not included in the statistical analysis due to insufficient n-size ($N = 4$), women's neuroendocrine and physical performance responses trended similarly to those observed for men, except for testosterone, which remained within normal ranges for women across all three timepoints. Due to the paucity of research in this subject population within the context of SERE training, women's data are included in **Table III** for reference.

DISCUSSION

The main finding of this investigation was the magnitude of cumulative stress experienced during SERE, which was evident in the significant elevations in neuroendocrine hormonal

Table II. Men's Neuroendocrine and Physical Performance Responses to SERE Stress.

	BASELINE (T1) ($N = 20$)	STRESS (T2) ($N = 20$)	RECOVERY (T3) ($N = 20$)	NORMAL RESTING RANGE
Epinephrine ($pmol \cdot L^{-1}$)	348.74 (± 140.02)	593.77 (± 205.39)*	343.57 (± 78.63)†	170 - 520 $pmol \cdot L^{-1}$
Norepinephrine ($pmol \cdot L^{-1}$)	2323.65 (± 458.67)	6758.45 (± 2351.21)*	4218.90 (± 1420.80)*†	1270 - 2810 $pmol \cdot L^{-1}$
Dopamine ($pmol \cdot L^{-1}$)	96.49 (± 30.78)	275.72 (± 135.09)*	172.71 (± 97.74)*†	0 - 196 $pmol \cdot L^{-1}$
Cortisol ($nmol \cdot L^{-1}$)	122.70 (± 49.79)	766.86 (± 157.87)*	333.84 (± 128.30)*†	50 - 410 $nmol \cdot L^{-1}$
Testosterone ($nmol \cdot L^{-1}$)	14.83 (± 4.66)	5.50 (± 4.06)*	6.81 (± 2.66)*	14 - 28 $nmol \cdot L^{-1}$
Neuropeptide Y ($pg \cdot mL^{-1}$)	348.16 (± 88.70)	328.42 (± 139.56)	146.16 (± 47.47)*†	Not established
Vertical Jump (cm)	56.71 (± 13.49)	55.25 (± 14.68)	N/A	N/A
Dominant Handgrip (kg)	50.03 (± 8.59)	51.50 (± 6.75)	N/A	N/A
Nondominant Handgrip (kg)	50.18 (± 8.98)	50.30 (± 8.34)	N/A	N/A
Body Mass (kg)	83.73 (± 12.88)	77.92 (± 12.24)*	78.57 (± 12.36)*	N/A

* Significant differences from baseline (T1) timepoint ($P \leq 0.05$). †Significant differences from stress (T2) timepoint ($P \leq 0.05$). Data are presented as mean (± SD).

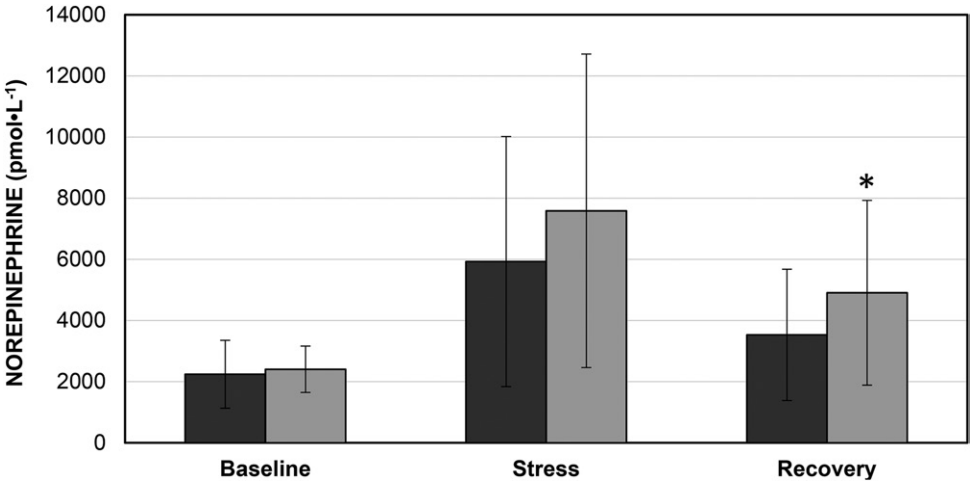

Fig. 1. Mean norepinephrine concentrations (pmol · L^{-1}) in the high fit ($N = 10$) and low fit ($N = 10$) groups at baseline (T1), stress (T2), and recovery (T3). High fit group: dark gray columns. Low fit group: light gray columns. * = Significant differences between groups ($P \leq 0.05$). Error bars at each time point denote standard deviation from the mean.

concentrations in "resting" (i.e., in the absence of exercise) blood samples at the stress assessment (T2), which had not fully recovered 24 h thereafter (T3). This, combined with reductions in serum testosterone, was indicative of acute hypogonadal function in men, as testosterone concentrations remained low for 24 h after T2. An unexpected finding was the lack of elevation in plasma NPY at T2 relative to baseline (T1) concentrations, with a sharp drop in the recovery period (T3). Despite the effects of cumulative stressors and a significant loss of body mass over the course of SERE training, no significant reductions in physical performances were observed. The magnitude of plasma norepinephrine response was influenced by physical fitness level with faster recovery and sympathetic control in fitter individuals. Physical fitness level also influenced NPY response at recovery, with higher NPY values observed in fitter subjects.

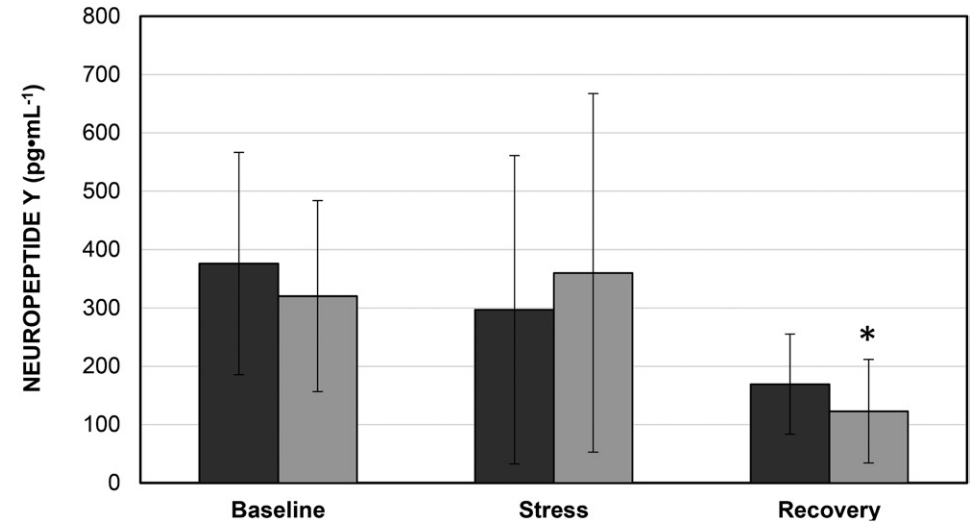

Fig. 2. Mean neuropeptide Y concentrations (pg · mL^{-1}) in the high fit ($N = 10$) and low fit ($N = 10$) groups at baseline (T1), stress (T2), and recovery (T3). High fit group: dark gray columns. Low fit group: light gray columns. * = Significant differences between groups ($P \leq 0.05$). Error bars at each time point denote standard deviation from the mean.

Catecholamines regulate a host of different physiological effects in the body, from increases in heart rate and blood pressure to energy release and blood flow to the skeletal muscle, all as part of the "fight or flight" response, especially when over-stimulated by unique stressors.[8] Prior work in SERE observed increases in norepinephrine response under high-stress conditions.[22] The results of the present research are in line with these findings, as significant elevations in norepinephrine were observed at T2, which had not re-equilibrated to resting concentrations by T3. The continued elevation in norepinephrine at the recovery timepoint is indicative of the high magnitude of adrenal stress experienced during the SERE course and may also reflect competing demands related to sleep deprivation, energy requirements and psychological coping mechanisms.[2,16,38] Alternatively, it is quite possible that the continued elevation in norepinephrine concentrations at recovery reflects a potential enzymatic slowing of biosynthetic processes in the conversion of norepinephrine to epinephrine.[4,14]

The classic hormone epinephrine, representing the rapid responder of the "fight or flight" response, was significantly elevated at T2, yet quickly re-equilibrated to T1 values after 24 h of recovery (T3). Such a rapid return to homeostasis demonstrates the tight homeostatic control for adrenal medullary chromaffin secretions. As part of the adrenergic response, proenkephalin fragments are also secreted from the adrenal medulla, which are involved in analgesia and immune modulation, especially of β cells.[5,35] Thus, the drop in epinephrine secretion to normal values may represent a concomitant elevation of proenkephalin fragments to address recovery needs.[15] Furthermore, it is possible that the β2 adrenergic receptors might have been downregulated by the demands of the SERE course, yet this is not consistent with the subsequent lack of change in neuromuscular performances at T2.[10]

After more than three decades, the role of peripheral plasma dopamine still remains unclear.[39] A unique finding in this study was the significant elevation of dopamine in "resting" (i.e., in the absence of exercise) conditions at T2, which had not fully recovered

Table III. Women's Neuroendocrine and Physical Performance Responses to SERE Stress.*

	BASELINE (T1) ($N = 4$)	STRESS (T2) ($N = 4$)	RECOVERY (T3) ($N = 4$)	NORMAL RESTING RANGE
Epinephrine (pmol · L^{-1})	234.69 (± 88.77)	361.59 (± 155.50)	182.84 (± 82.28)	170 - 520 pmol · L^{-1}
Norepinephrine (pmol · L^{-1})	2291.50 (± 359.95)	6510.97 (± 2089.63)	3855.45 (± 1267.36)	1270 - 2810 pmol · L^{-1}
Dopamine (pmol · L^{-1})	86.99 (± 13.32)	169.62 (± 36.03)	133.74 (± 30.77)	0 - 196 pmol · L^{-1}
Cortisol (nmol · L^{-1})	139.79 (± 60.61)	937.37 (± 276.37)	251.07 (± 60.54)	50 - 410 nmol · L^{-1}
Testosterone (nmol · L^{-1})	1.10 (± 0.17)	1.79 (± 0.26)	0.97 (± 0.22)	0.52–2.43 nmol · L^{-1}
Neuropeptide Y (pg · mL^{-1})	356.67 (± 53.47)	317.25 (± 92.21)	174.25 (± 26.55)	Not established
Vertical Jump (cm)	39.37 (± 6.78)	35.88 (± 7.37)	N/A	N/A
Dominant Handgrip (kg)	33.50 (± 3.20)	30.00 (± 4.95)	N/A	N/A
Body Mass (kg)	67.19 (± 5.11)	63.50 (± 5.18)	63.28 (± 5.02)	N/A

* Women's data are presented for reference (data were not included in statistical analysis). Data are presented as mean (± SD).

at T3. An exercise-induced stress response of dopamine in peripheral circulation was first demonstrated in extreme short rest high intensity circuit resistance exercise protocols, with dopamine concentrations elevated 5 min following recovery.[14] In a subsequent study it was dramatically shown that dopamine is very dynamic in its plasma changes, with significant increases immediately prior to multiple sets of heavy resistance exercise, with continued increases between sets and remaining elevated for 30 min into recovery, demonstrating an elongated recovery phase.[9] Extraordinary in the present investigation was that at T2 and 24 h later at T3, dopamine concentrations represent a relatively long-term recovery that is not yet complete from a homeostatic regulatory perspective. It has been postulated that enzymatic inhibition limits the conversion of dopamine to norepinephrine and thus also may have masked the true elevation of both norepinephrine and epinephrine.[4,14] High stress events, such as off road motor cross, have also resulted in dramatic elevations in urinary dopamine concentrations associated with oxidative stress, indicating a stress-related feature of increases in peripheral levels of dopamine.[3] Sleep deprivation of 24 h has been shown to increase norepinephrine and dopamine, but not epinephrine, supporting that sleep stress may also have played a role in the elevation of peripheral dopamine, yet the underlying mechanisms beyond enzymatic pathways in peripheral circulatory changes remain to be determined.[19]

Interestingly, at the onset of SERE training, serum cortisol values might be considered on the low end of normal, suggesting that accumulated stress prior to the course was not significant from the current duty stations. The sharp increase in cortisol at T2 reflects the impact of cumulative stressors in creating a catabolic hormonal milieu which was further exacerbated by the captivity training scenario (i.e., interrogation and solitary confinement) prior to T2. The effects of caloric restriction, i.e., low blood glucose after several days of food deprivation and increased energy expenditure, would cause an increase in resting cortisol concentrations, as cortisol stimulates gluconeogenesis and inhibits other glucose cellular expenditures to protect glycogen stores and promote the breakdown of fat stores for energy.[26] The cortisol elevations observed in the present investigation are thus expected, given that cortisol increases are associated with anticipatory stress, mental and physical challenges, and strenuous military training scenarios where high stress, increased energy expenditure, decreased caloric intake and sleep deprivation are common.[1,17,24]

With extreme oxidative stress or high amounts of physical exertion over extended time periods, reductions in testicular function can compromise plasma testosterone concentrations in men. In this investigation, we observed a significant decrease in testosterone in men from within normal range at T1 to very low testosterone concentrations at T2, which may be classified as an acute hypogonadal response. Testosterone did not return to normal resting concentrations at T3, reflecting a slow recovery in concert with the remaining higher concentrations of cortisol, making for a continued catabolic hormonal environment. Our findings are in line with previous research which has shown that both strenuous military training and heavy endurance exercise result in increased cortisol and decreased testosterone concentrations in men.[12,17,24] In men, with high levels of stress and physical activity, greater testosterone use and turnover at the androgen receptor levels are observed. Thus, the low (but within normal resting ranges) testosterone concentrations at T1 may well have been related to the type (i.e., endurance exercise) or total volume of physical activity being conducted prior to SERE. Other potential influences contributing to the clinically low resting testosterone values observed at T2 and T3 are sleep deprivation and inadequate caloric intake relative to energy expenditure.[17,21,33]

Unexpectedly, we observed no elevation in neuropeptide Y concentrations from T1 to T2 despite the magnitude of adrenergic and adreno-cortical arousal at the stress assessment (T2). Prior SERE research has shown that NPY concentrations increase during periods of "uncontrollable stress," and that elevations in NPY are correlated with concomitant increases in catecholamines and cortisol.[20,22,23] This is, to our knowledge, the first study to show a possible dysregulation for NPY and adrenal function at the baseline timepoint (T1), as NPY values were elevated relative to the low serum cortisol and plasma catecholamine values seen this timepoint. At T2 the high NPY response pattern appears more consistent with adrenal stress elevations. NPY was correlated with epinephrine ($R = 0.49$, $P = 0.03$) and norepinephrine ($R = 0.44$, $P = 0.05$) at this timepoint.

Although we obtained a T1 resting blood sample on the first day of SERE training, it is possible that NPY concentrations were already elevated as a positive "coping" strategy, especially for anxiety, in anticipation of the ensuing SERE training course. The upregulation of this peptide may allow for an adaptive strategy in coping with stress by reducing cardiovascular tone

and suppressing anxious behavior.[6,37] Again, the NPY concentrations at T1 are an interesting finding given that adrenal stress hormone concentrations were within normal ranges at T1. Furthermore, although NPY was correlated with epinephrine and norepinephrine at T2, and with dopamine at T3 ($R = -0.49$, $P = 0.03$), no correlations were observed at baseline, similar to the findings of a previous investigation.[23] This apparent disassociation suggests other pathways may be operational in its response.[37] The sharp drop in NPY at T3 could be a reflection of maladaptive NPY responses after cessation of a period of high stress, i.e., inability of NPY to recover quickly to resting values.

We had the unique opportunity to be among the first to gain data on physical performances (i.e., neuromuscular performance) during U.S. Navy SERE training. Although one other recent investigation of Polish SERE training demonstrated significant pre to post decreases in performance (i.e., handgrip test, motor adjustment skills, dynamic balance), no performance measures were obtained during the acute stress portions of that training course.[34] Furthermore, it should be noted that international SERE courses may vary greatly from U.S. SERE training courses, especially the Navy SERE course, therefore caution should be used when making direct comparisons. Another recent investigation examined heart rate responses to SERE training, but did not include other physical performance measures.[18] In the present investigation, it is possible that the catecholamine elevation at T2 (almost threefold increase from T1) was responsible for the maintenance of physical performance from T1 to T2 as epinephrine has been shown to enhance the myosin motor and neuromuscular performance in some men.[9] Additionally, for the vertical jump, the reduction in body mass from T1 to T2 may have contributed to maintenance of vertical jump height. It is also possible that other physical performance measures, such as a neuromuscular endurance test, may have resulted in differences in performance. Once again, due to the constraints of the SERE training course and our desire to maintain the integrity of the SERE plan of instruction, more invasive or time-intensive performance measures were not possible to implement in our study design.

With regards to the influence of physical fitness level on neuroendocrine responses, we observed no differences between high fit and low fit groups for norepinephrine at T1 or T2. However, fitter subjects had lower norepinephrine values at T3 when compared to less fit subjects. Previous work demonstrated that Special Forces soldiers had an increased norepinephrine response during a high stress phase of SERE training when compared to non-Special Forces soldiers (Rangers, Marines), with quicker return to baseline concentrations, although one cannot make a direct comparison between these results and the present investigation.[22] One would hypothesize that higher levels of fitness would result in greater neuromuscular control by the sympathetic nervous system, resulting in lower norepinephrine values. This hypothesis has some support in the study of exercise training of soldiers as it has been demonstrated that lower norepinephrine concentrations were observed in response to submaximal exercise intensities, but in response to maximal exercise the sympatho-adrenal response or norepinephrine values were higher.[13,38] Different from the norepinephrine response, level of fitness did not influence the epinephrine response pattern.[22] Our results were consistent with prior work which had also reported no differences in epinephrine response between Special Forces and conventional soldiers.[22]

NPY is thought to have a protective role in stress and has been implicated as a factor in "resilience" or "hardiness," with more resilient or fit individuals typically having higher NPY concentrations when compared to less fit/resilient individuals.[23,27] Physical fitness influenced the pattern of NPY response, with higher NPY values in the high fit group at recovery. Prior work has shown that NPY concentrations were higher during "uncontrollable stress" in Special Forces soldiers when compared to conventional soldiers.[22] An associated study found that NPY concentrations in Special Forces soldiers had returned to baseline values during recovery, whereas concentrations remained below baseline values in non-Special Forces soldiers.[23] Although caution must be used in making direct comparisons between these studies and the results of the present investigation, one could hypothesize that differences in NPY response could be related to military training level or physical fitness level. This hypothesis finds support in the present investigation, which observed differences in NPY at the T3 recovery timepoint in sailors and Marines who differed in level of physical fitness as measured by physical fitness test scores and baseline handgrip test scores.

In summary, the results of this investigation demonstrate that the Navy SERE course resulted in a high magnitude of stress evident in neuroendocrine responses and a significant reduction in body mass, but with no associated reductions in physical performance measures. Additionally, fitness level may offer some degree of protection from cumulative stressors experienced during military training courses such as SERE. In the present study, men with higher fitness levels had a quicker recovery of adrenergic responses, specifically norepinephrine and NPY, which could point to improved recovery and immune capabilities and thus positive effects on resilience. Important to military readiness in the context of military training and operations, it appears that physical fitness level and stress status at the onset of military training may influence the initial recovery outcomes during Navy SERE. Longer-term recovery implications and whether these findings have clinical relevance remain important areas for future research. Our research also revealed interesting findings regarding the role of NPY in the stress response and a potential dysregulation for NPY and adrenal stress at the baseline timepoint of measurement. More research is required to elucidate the relationship between NPY and adrenal stress responses, particularly as it relates to fitness level, immune function and longer-term recovery.

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