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The following component part numbers comprise the compilation report:

ADP010649 thru ADP010658
Acute Recovery of Physiological and Cognitive Function in U.S. Army Ranger Students in a Multistressor Field Environment

by

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1. ABSTRACT

The time course for soldier recovery and reentry to the battlefield following high intensity direct action missions is of importance to unit commanders and military planners. It also provides a critical background understanding for medical researchers investigating approaches to extend the limits of soldier physical and psychological endurance. This report summarizes findings for soldiers followed through two recovery periods, during and after, a prolonged exhaustive military activity, the U.S. Army Ranger course. Within the course, with a modest increase in sleep and energy intake for 7 days, the soldiers demonstrated recovery of some cognitive function (e.g., decoding and pattern analysis) and acute metabolic/stress markers (e.g., serum testosterone, IGF1, and triiodothyronine). More complex intellectual processes (e.g., reasoning), other biochemical indicators (e.g., hyperlipidemia, serum cortisol), and cell-mediated immune function (e.g., in vitro PHA-stimulated T-lymphocyte proliferation) demonstrated progressive changes in response to the cumulative stress and were unaffected by the partial cessation of stressors during the course. Five weeks after the course, all of these parameters demonstrated recovery, or even overshoot. These data illustrate the remarkable resilience of fit young soldiers and demonstrate that a brief period of increased sleep and feeding partially restores soldiers before reentry to combat.

2. INTRODUCTION

The multiple stressors in a combat environment produce an overall stress burden with consequences similar to those reported in athletic "overtraining." Overtraining is defined here as unusually high intensity effort with inadequate physiological recovery, leading to degraded military performance. Problems associated with such prolonged exhaustive military activities, or "military overtraining," include a reduction in physical capabilities and cognitive function, and possibly a reduced ability to recover from infection and injury. This overtraining phenomenon occurs even in the absence of an infectious disease or traumatic injury overlay.

The earliest functional recovery of soldiers following intensive and stressful missions is of great importance as a force multiplier. The combination of stressors such as high energy flux, energy deficit, inadequate restorative sleep, anxiety, ambient heat etc., have been shown to produce critically important physiological consequences which can produce critical functional impairments (1,2). The stress and fatigue responses produce neuroglycopenic symptoms marked by suboptimal cognitive function. Resultant errors in interpretation and judgement can produce catastrophic failures in combat, such as misidentification of friendly forces and selection of a poor course of action. Stress-induced reductions in immunocompetence increase susceptibility to infectious disease, with the possibility of performance degradations or incapacitation of entire units. Reduced immune function may also be an early indicator of other impairments in soldier stress.

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defenses. Thus, cognitive and immunological status are critical factors in the decision to return soldiers to duty after an intensive mission.

This report describes the pattern of recovery of measures that reflect these two critical capabilities and compares them to patterns of change in metabolic/stress markers. This type of descriptive study is important to subsequent pursuit of safe and effective strategies to prevent decrements or enhance recovery of performance such as identification of critical timepoints for sleep and refeeding, and use of pharmacological enhancers, neurotransmitter precursors (e.g., tyrosine and choline), and immune function boosters (e.g., antioxidants).

3. THE RANGER COURSE AS A MODEL OF MILITARY OVERTRAINING

3.1 Course description

The U.S. Army Ranger course is designed to train young infantry leaders through discovery of their strengths and weaknesses under stress and development of strategies to cope with leadership challenges in this environment. This course deliberately limits food intake and sleep and includes other environmental stressors which are components of realistic tactical training (Table 1).

<table>
<thead>
<tr>
<th>Stressor (reference)</th>
<th>Description &amp; method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food restriction (2)</td>
<td>Deficit=1000 kcal/d for 8 wks, from body composition change</td>
</tr>
<tr>
<td>Sleep restriction (3)</td>
<td>Sleep=3.6 h/d for 8 wks, from 24 h wrist activity monitors</td>
</tr>
<tr>
<td>Physical exertion (4)</td>
<td>Energy expenditure=4000 kcal/d, up to 6000 kcal/d, from $^{2}\text{H}_{2}^{18}\text{O}$</td>
</tr>
<tr>
<td>Weather (1)</td>
<td>Avg daily maximum temperature=30 C; relative humidity=\sim80%</td>
</tr>
<tr>
<td>Medical problems (5)</td>
<td>Blisters, insect bites, sprains &amp; strains, cellulitis and respiratory infections</td>
</tr>
<tr>
<td>Evaluation anxiety</td>
<td>(unquantified)</td>
</tr>
</tbody>
</table>

The Ranger Course is divided into 4 phases of approximately 2 weeks each and exposes soldiers to training in four different environments: temperate forest, desert, rough "mountain" terrain, and coastal swamp. Each phase begins with a few days of adequate feeding and increased sleep while soldiers are taught new skills. This is followed by 7-10 days with one meal per day and more constrained opportunities for sleep, during realistic small unit operations. These typically involve 8-12 km patrols with loaded rucksacks (~35 kg).

3.2 Course stressors

The energy deficit is actually produced with a repeated food restriction and refeeding (a mixed diet, with caloric content divided into approximately 50% carbohydrate, 35% fat, 15% protein) in the four phases through the course (Figure 1). This repeated semi starvation and refeeding produces a profound hunger stressor but without the gastric upset which occurs with fasting in stressful conditions. Energy expenditure fluctuates throughout the course, with the highest measurements by doubly-labeled water (6,000 kcal/d), occurring in the first half of the mountain phase training, when abseiling and climbing techniques are taught. The lowest energy expenditure occurs towards the end of the course, reflecting behavioral and physiological efficiencies induced by the energy deficit.
Based on data from wrist-worn activity monitors, sleep averaged 3.6 h/d in two separate studies (3). This increases slightly during the first half of each of the four course phases (4.0 vs 3.2 h)(3). Increased amounts of sleep in the last two-week phase of training (4.3 ±0.8 h/d) probably reflect an unavoidable increase in napping during training.

### 3.3 Functional deficits

Some of the key consequences that have been described in Ranger training are summarized in Table 2. Although there is a substantial and prolonged energy deficit, nutritional biochemistry and physical exams at the end of the 1991 study demonstrated no deficiencies in any key vitamins or nutrients; only retinol concentrations were marginally reduced from baseline and below normal limits (1,2). Protein intake was at least 50 g/d on days with only a single meal. Thus, the primary consequences of the nutritional stressor are an uncomplicated energy deficit. The approaching depletion of available fat energy stores produces an increase in cortisol and an increased utilization of body protein to meet energy requirements (8).

<table>
<thead>
<tr>
<th>Function (reference)</th>
<th>Description &amp; indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy metabolism (1)</td>
<td>↓ glucose availability (fasting glucose -20%, insulin -40%); ↓ metabolic rate (↓ T3); ↑ counterregulatory hormones (growth hormone &amp; cortisol)</td>
</tr>
<tr>
<td>Protein status (2)</td>
<td>↑ protein catabolism (-6% of total FFM) without protein deficiency (↓ prealbumin, ↔ total proteins, ↑ RBP)</td>
</tr>
<tr>
<td>Physical (2,6,7)</td>
<td>↓ max aerobic capacity (-14%); ↓ max lift strength &amp; vertical jump (-20%)</td>
</tr>
<tr>
<td>Cognitive (2)</td>
<td>↓ speed in decoding -33%, pattern analysis -15%, and reasoning -20%</td>
</tr>
<tr>
<td>Immunological (1,2)</td>
<td>↓ T- &amp; B-lymphocyte proliferation response in vitro to mitogens; ↓ IL6</td>
</tr>
</tbody>
</table>
Cumulative stress responses and fatigue near the end of the course produce a mental drowsiness referred to as "droning." Cognitive deficits have been studied in several Ranger studies (2,9). In the 1992 study, rote memorization of a short list of code words was relatively unaffected by severe food and sleep restriction. However, other tests indicated that accuracy on tasks such as decoding map coordinates or analyzing maps could be sustained under severe food and sleep restriction, but predicted that soldiers would take 1.5 times longer than normal to complete the tasks. The ability to make logical inferences or develop a course of action, would also take longer than normal (2).

Immunological function has been primarily assessed in Ranger students using in vitro proliferative activity of lymphocytes. No consistent results were obtained in the 1991 study using delayed hypersensitivity tests with antigens to 7 microorganisms. However, phytohemagglutinin (PHA)-stimulated T-lymphocyte activity demonstrated marked and reproducible declines in both the 1991 and 1992 studies, with the largest attenuation in response associated with periods of highest energy expenditure and deficit. Interleukin-2 receptor and IL2 secretion from stimulated lymphocytes demonstrate recoveries before the end of the course and in advance of recovery of the T-lymphocyte proliferative activity (1).

Ranger students are more susceptible to infectious diseases, including problems with cellulitis, uncommon in other soldiers (5). Another problem that is uncommon in healthy adults, Streptococcal pneumonia, has been a significant problem for winter Ranger students (5). A limited trial was made with administration of prophylactic bicillin to entire classes in an effort to reduce the infectious disease problems (5). A modest increase in food intake appears to attenuate the infection rate and some of the observed decrements in immune function measures (2). The consequences of this multistressor environment can themselves further contribute to the total stress burden of the individual student (e.g., injuries which occur through errors made by fatigued soldiers and illnesses which result from reduced immunological defenses).

4. DESCRIPTION OF RECOVERY STUDY

This report summarizes findings from new data analyses of the 1992 study (2) concerning recovery within one phase of the course and following the course at one and five weeks. Originally, there was concern that Rangers may have lasting impairments stemming from the rigors of the training. Six months after the 1991 study, eight Rangers were reexamined with detailed physical exams and recent medical histories and for physical assessments (1). These soldiers were all fully restored to baseline health and strength; however, they described profound impairments in the first few weeks after training. This recovery study design was built into the 1992 study to further examine the pattern of acute functional recovery within and following the course.

Data for the 10 soldiers participating in the 1992 study are shown in Table 3. Limited data was obtained from blood samples collected from another 9 course finishers at one week after the end of the course; no other data was available on these soldiers. Table 3 illustrates the large reduction in body fat stores, supplying 85-90% of the energy deficit. It also shows the large rebound in fat stores representing 2000 kcal/d excess energy after the course, with unrestricted rest and food intake (9).

<table>
<thead>
<tr>
<th>Measure</th>
<th>B/L</th>
<th>4 wk</th>
<th>5 wk*</th>
<th>8 wk</th>
<th>+5 wk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body wt (kg)</td>
<td>73.9±2.9</td>
<td>68.1±2.3</td>
<td>73.9±1.5</td>
<td>65.5±2.3</td>
<td>76.3±3.0</td>
</tr>
<tr>
<td># Fat wt (kg)</td>
<td>9.5±1.5</td>
<td>----</td>
<td>----</td>
<td>5.3±0.9</td>
<td>13.7±1.2</td>
</tr>
<tr>
<td># FFM (kg)</td>
<td>64.4±1.6</td>
<td>----</td>
<td>----</td>
<td>60.2±1.9</td>
<td>65.5±2.2</td>
</tr>
</tbody>
</table>

*Recovery periods; # calculated from body weight and % body fat assessed by dual-energy x-ray absorptiometry
During the first 5 days after the end of the course, soldiers only increased sleep duration to 6.5 h/d. They also demonstrated a reduced quality of sleep over that measured during the course, with greater sleep fragmentation and greater movement during sleep (3).

5. RECOVERY OF COGNITIVE FUNCTION

Soldiers were tested on four tasks that are commonly used in cognitive assessment batteries: information processing, perceptual processing, reasoning, and memory (11). Although the tasks were all administered as timed pencil-and-paper tests and all yielded dependent measures of speed and accuracy, the cognitive processes measured by these tasks differ in complexity, level of processing, and simplicity of response.

Decoding. The decoding task was used to measure speed of information processing. It was a straightforward task, requiring the soldier to translate geometric figures into numbers using a code key. This task could be compared to the task of authenticating military communications. Soldiers could check their work for accuracy as they completed the test.

It is clear from Figure 2 that there was substantial recovery on the mid-mountain phase test and on the post-training test, relative to the desert and jungle phase tests, respectively, and that the degree of recovery was similar in both cases. Soldiers completed approximately 1.4 times as many problems on the post-training test as they had on the jungle phase test. This is supported by the ANOVA, which showed that only the training intensity was statistically significant.

Figure 2. Results of the cognitive function tests for 10 soldiers followed through the Ranger course and subsequent recovery. (Results are shown as % correct responses).
**Pattern analysis.** The pattern analysis task was used to measure speed of perceptual processing. It was similar to the decoding task; however, the task required a higher order skill. Soldiers were required to analyze complex geometric figures to determine if they contained a simpler figure found in the code key. This task could be compared to the task of analyzing unit symbols on a military map.

Performance on the pattern analysis task was similar to that on the decoding task. Figure 2 shows the same pattern of recovery as for the decoding task. Soldiers completed approximately 1.25 times as many problems on the post-training test as they had on the jungle phase test. Only the main effect of training intensity was significant in the ANOVA.

**Reasoning.** The reasoning task was used to measure speed of inferential logic. It required soldiers to rapidly determine whether a one-sentence description of the order of a simultaneously presented pair of letters was logically true or false. For example: AB, A is not followed by B (true or false?). This task could be compared to the task of analyzing a plan of action to determine its agreement with a field operations order. An interesting interaction effect was seen in the reasoning data. As shown in Figure 2, performance on the reasoning task did not recover on the mid-mountain phase test, but did recovery on the post-training task. Soldiers completed approximately 1.2 times as many problems on the post-training test as they had on the jungle phase test. The interaction effect was significant but the two main effects were not significant. Pair-wise comparisons showed a statistically significant recovery of performance only on the post-training test, compared to the jungle phase test (p<0.02). These data suggest that the more complex intellectual process of reasoning recovers only when food and sleep are unrestricted.

**Memory.** The memory task was used to measure accuracy of memorization. It required soldiers to rapidly memorize nine pairs of words. Military operations often require memorization of seemingly random lists of word, such as challenge and pass words, codenames for objectives, landmarks, operations, etc. The memory task was divided into two parts: presentation and recall. In the presentation portion, soldiers were given a pair of words in a mnemonic sentence (i.e., nine sentences - 18 words). In the recall portion, soldiers were given a list of 15 words and asked to mark "true," if the word were from the previous set of 18 words and "false," if it were not. Among the 15 words, nine were always from the previous list and six were not, although soldiers were never told of this relationship. The reasoning task was administered between the two parts of the memory task, preventing soldiers from rehearsing words during the delay between presentation and recognition testing.

Performance on the memory test was apparently unaffected by severe food and sleep restriction. There were no statistically significant differences in the ANOVA (Figure 2).

### 6. RECOVERY OF CELL-MEDIATED IMMUNE FUNCTION

PHA-stimulated T-lymphocyte activity declined significantly from baseline to the beginning of the mountain phase but did not increase in response to refeeding within the course (Figure 3). This response was restored to baseline by the end of the course and was not significantly different at one week post, but it was substantially higher than baseline at 5 weeks post (2-way ANOVA; p<0.05). This suggests that other factors in the course beside energy and sleep deficits, such as total energy expenditure, are responsible for the suppression of cell-mediated immune function. There may also be a compensatory recovery which would occur despite continuation of the stressors during the course. The hyperresponsiveness noted at 5 weeks post supports this.
7. **RECOVERY OF METABOLIC MARKERS**

Morning blood samples were drawn from soldiers following overnight fasting, processed and frozen onsite for later analysis, with all samples for individuals analyzed in the same assay. Biochemical markers of stress and metabolic status were used to assess recovery during and after the course.

**Thyroid axis & other metabolic markers.** Classical markers of protein-energy malnutrition, such as IGF1 (12) and triiodothyronine (13), demonstrated prompt and complete return to baseline with refeeding in the mid-mountain phase, and a significant rebound in the 5 week post-recovery sample. These differences in the magnitude of recovery were reflected in significant interactions between training intensity and course phase (2-way ANOVA, p<0.05). Reduction in thyroid activity is at least partially adaptive in the hypocaloric setting (14) and with increased risk of infection (15). Other aspects of thyroid function responded as expected in energy deficiency, with only a modest reduction and slower recovery of thyroxine. Prompt reduction in TSH following refeeding periods indicated regulation by higher centers but this differs from short-term studies (16).

Ferritin and binding proteins (TBG, SHBG) demonstrated the same pattern of acute recoveries, with significant changes in both recovery periods. Insulin is known to be a key regulator of the binding proteins (17), and prompt suppression of these two proteins during recovery indicates a return to normal carbohydrate metabolism.

**Gonadal axis as a generalized stress marker.** Testosterone promptly returned to baseline in both refeeding periods, supporting the concept that energy deficiency is a most critical stressor in this course. Although sleep was increased during these recovery periods, sleep deprivation is not as important in the suppression of testosterone (18). Anxiety stress produces a sustained suppression of testosterone during military training but ambient heat stress has no effect (Friedl, unpublished, 1985). As with the thyroid axis, the observed suppression of LH reflects a higher level regulation (19).
Table 4. Serum hormone levels (means±SEM) during and after Ranger training (n=10).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>B/L</th>
<th>4 wk</th>
<th>5 wk*</th>
<th>8 wk</th>
<th>+5 wk*</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGF1 (ug/L)</td>
<td>205±16</td>
<td>101±7</td>
<td>185±21</td>
<td>88±7</td>
<td>253±11</td>
</tr>
<tr>
<td>T3 (nmol/L)</td>
<td>1.84±0.16</td>
<td>1.55±0.11</td>
<td>1.96±0.07</td>
<td>1.47±0.08</td>
<td>2.46±0.10</td>
</tr>
<tr>
<td>T4 (nmol/L)</td>
<td>101±5.9</td>
<td>84±4.3</td>
<td>77±3.1</td>
<td>82±5.0</td>
<td>101±5.8</td>
</tr>
<tr>
<td>TSH (mU/L)</td>
<td>2.4±0.2</td>
<td>3.7±0.5</td>
<td>3.0±0.3</td>
<td>4.5±0.5</td>
<td>2.7±0.4</td>
</tr>
<tr>
<td>TBG (nmol/L)</td>
<td>20.3±1.0</td>
<td>22.9±0.8</td>
<td>20.7±1.1</td>
<td>24.0±1.5</td>
<td>18.4±0.9</td>
</tr>
<tr>
<td>T (nmol/L)</td>
<td>16.3±1.6</td>
<td>4.3±0.5</td>
<td>14.6±0.8</td>
<td>2.2±0.9</td>
<td>19.3±3.2</td>
</tr>
<tr>
<td>LH (U/L)</td>
<td>8.0±0.7</td>
<td>6.1±0.6</td>
<td>6.3±0.5</td>
<td>4.2±0.9</td>
<td>8.6±0.7</td>
</tr>
<tr>
<td>SHBG (nmol/L)</td>
<td>24.6±2.4</td>
<td>48.5±3.9</td>
<td>28.0±2.4</td>
<td>44.0±4.0</td>
<td>19.7±1.2</td>
</tr>
<tr>
<td>F (nmol/L)</td>
<td>441±22</td>
<td>417±31</td>
<td>550±50</td>
<td>706±34</td>
<td>507±51</td>
</tr>
<tr>
<td>HDLC (mmol/L)</td>
<td>1.3±0.1</td>
<td>1.7±0.1</td>
<td>1.9±0.1</td>
<td>2.3±0.2</td>
<td>1.2±0.2</td>
</tr>
<tr>
<td>Ferritin</td>
<td>82±14</td>
<td>128±17</td>
<td>91±20</td>
<td>163±17</td>
<td>47±8</td>
</tr>
</tbody>
</table>

*Recovery periods
Note:  IGF1=insulin-like growth factor 1; T3=triiodothyronine; T4=thyroxine; TSH=thyroid-stimulating hormone; TBG=thyroid binding globulin; T=testosterone; LH=immunoreactive luteinizing hormone; SHBG=sex hormone binding globulin; F=cortisol; HDLC=high density lipoprotein cholesterol.

Markers of more severe metabolic stress. Cortisol demonstrated the largest rise in the second half of the course, as did other markers such as HDL-cholesterol (and the other cholesterol fractions), indicating the cumulative metabolic stress as body fat stores become substantially reduced (20). The period of refeeding during the course was inadequate in restoring levels to baseline but, 5 weeks after the course, all values were returned to initial concentrations (2-way ANOVA, p<0.05). In the alternate subsample of students, cortisol was restored within the first week after the end of the course. This indicates a difference between the two recovery periods with respect to adrenal activation, possibly reflecting the difference of high intensity activity during the course and virtual cessation of physical exertion in the first week after the course.

8. CONCLUDING REMARKS

The most important observation in this study was that a period of refeeding, along with a small increase in sleep, provided only a transient restoration of some measures or functions. Even with continuation of other course stressors, simple cognitive tasks were restored to baseline, as were generalized stress markers such as serum testosterone and metabolic markers such as triiodothyronine and IGF1. Thus, the acute improvement in metabolic status produced some short term functional restoration; however, these measures promptly returned to their place in a pattern of progressively larger change from baseline, following this within-course recovery period. Other measures were unchanged by this partial relief of course stressors, including indicators of cell-mediated immune function, reasoning capabilities, and metabolic markers such as ferritin and cholesterol subfractions.

By the end of the 8 week course, T-lymphocyte response was returned to baseline, even with continued stress; this demonstrated an overshoot from baseline by 5 weeks after the course. Cessation of stressors and a large positive energy balance produced a larger-than-baseline lymphocyte responsiveness when added to the compensatory recovery. Acute metabolic markers including triiodothyronine and IGF1 also demonstrate substantial rebound recoveries 5 weeks after the course, in concert with a body fat increase of 150% over baseline.

In summary, these findings suggest that 1) simple aspects of cognitive function may be susceptible to partial relief of the multiple stressors including increased feeding with acute metabolic recovery, 2) more complex cognitive functions such as reasoning are not, 3) the large reduction in immune function is either not
susceptible to refeeding or has a longer latency period than the 5-7 days in this recovery period, and 4) compensatory mechanisms correct the immunological deficit by the end of the course.

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This study was conducted in accordance with the principles of the Declaration of Helsinki and the explicit directives of Army Regulation 70-25, "Use of Volunteers as Subjects of Research." This study was approved by an Institutional Review Board at the U.S. Army Research Institute of Environmental Medicine, Natick, Massachusetts, and by the Human Use Review Office, Office of the Surgeon General, Department of the Army.

References


