# Exercise, Dehydroepiandrosterone (DHEA), and Mood Change: A Rationale for the "Runners High"?

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**ABSTRACT:** **Background:** Although exercise has been shown to improve mood and well-being, the precise mechanism remains unknown. Neurosteroids are important neuroactive molecules with demonstrated involvement in several neurophysiological and disease processes. Previous research has noted neurosteroid changes in dehydroepiandrosterone (DHEA) levels following exercise.

**Objectives:** To determine whether changes in DHEA levels are associated with mood improvement after exercise and whether there are any differences in the effects on younger and older individuals.

**Methods:** Individuals ≤ 50 years of age or › 65 years of age were recruited for study participation. Before and after 30 minutes of a standardized cycling regimen, each patient provided a blood sample and completed a questionnaire on mood and well-being.

**Results:** Findings confirmed a significant increase in DHEA levels post-exercise. A decrease in negative factors (fatigue, tension, depression, anger) and an increase in positive mood factors were noted. No difference in change of measures was noted between younger and older subjects. A positive correlation was noted between mood change and DHEA blood-level changes in older subjects. Among older males, DHEA appeared to be associated with mood change after exercise.

**Conclusions:** While preliminary, findings indicate a possible association between mood improvement following exercise and DHEA blood level changes. Understanding the biological mechanisms of exercise-induced mood changes is critical to utilizing exercise as a treatment for mood disorders.

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**KEY WORDS:** dehydroepiandrosterone (DHEA), exercise, mood, neurosteroid, runner's high

It is well-known that exercise is important in the improvement of mood and well-being; however, the precise mechanism for this finding remains unknown. "Runner's high," an exercise-induced altered state of consciousness sometimes experienced by endurance athletes, has been defined as "pure happiness, elation, a feeling of unity with one's self and/or nature, endless peacefulness, inner harmony, boundless energy and a reduction in pain sensation" [1]. Such descriptions reflect those described by individuals undergoing trance and drug states and include, at times, distorted perception, diminished awareness of surroundings, and profound introspective understanding [1]. While researchers have attempted to explain the phenomenon of runner's high by means of the "endorphin hypothesis" and endogenous opiate release, evidence is not strong for the theory and it has been challenged by data to the contrary. For example, it has been shown that β-endorphin is not able to cross the blood–brain barrier, thus the central effects of peripheral opioids most likely are not the source of the runner's high [2]. Despite various studies on the subject [1-3], including research on the endocanniboid system showing exercise induces increases in blood levels of anandamide that modifies various emotional and cognitive processes, no theory has proven satisfactory. Thus, the quest remains for a more definitive explanation of the runner's high phenomenon.

Previous studies, although limited in number, have noted increased levels of neurosteroids, including dehydroepiandrosterone (DHEA), with exercise [4-6]. The mechanisms contributing to this increase remain unknown. Neurosteroids are important neuroactive substrates with demonstrated involvement in several neurophysiological and disease processes. Since the term was first formulated in 1981 by Baulieu and Robel [7], the concept of neurosteroids has rapidly become important in the knowledge of neural systems and central nervous system (CNS) disease pathology.

Neurosteroids exhibit a wide range of neurotransmitter receptor activity and the effects influence neurophysiological processes. These activities becomes important for fine-tuning CNS functioning and indicate the critical role that neurosteroids play in normal and pathological operations. Arguably, the most important and widespread effect of neurosteroids may be noted in the gamma-aminobutyric acid (GABA) receptor, most notably the $GABA_A$ receptor [8]. In addition, neurosteroids may have various effects on the *N*-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA), kainate, glycine, serotonin, sigma type-1, and nicotinic acetylcholine receptors [8]. Since these neurotransmitters and receptors affect behavior and psychopathology, it is not surprising that neurosteroids have become a vital factor in the understanding of cognition, behavior, and general well-being.

However, whether changes in levels of DHEA following exercise are associated with improvement in mood and well-being (e.g., runners high) have yet to be investigated. These changes may indicate a theoretically plausible explanation considering the well-known mood enhancement effects of some neurosteroids, such as DHEA, as well as the demonstrated increase of DHEA levels following exercise.

The aim of this study is to investigate and explore whether there is any association between changes in blood levels of DHEA and mood and well-being following aerobic exercise. We investigated levels of DHEA rather than DHEA-S since the effects of acute exercise and DHEA's shorter elimination half-life were preferable for our purposes [6]. In addition, since levels of DHEA are lower in the elderly, we intended to explore whether effects of exercise on DHEA blood levels, mood, and general well-being would be any different in this sub-population compared to younger individuals.

## PATIENTS AND METHODS

Males and females between the ages of 18 and 50 years as well as those over 65 years of age who were in good physical health were recruited for our study participation. Due to the physically demanding nature of the study, study participants over the age of 65 years were required to provide a letter from their physician of their physical health to participate. The study was approved by the ethics review board at Beer Yaakov Mental Health Center.

Following signed informed consent and completion of a brief demographic questionnaire, study participants were asked to complete a short battery of rating scales assessing their current mood and energy state. In addition to the pre-intervention evaluation, subjects provided a 5 ml sample of peripheral blood for DHEA and cortisol analysis. Completion of the questionnaire was followed by a period of 30 minutes of aerobic exercise on a stationary exercise bicycle. The nature of the exercise was standardized by means of medium perceived effort according to subjective self-report on the Borg scale [9]. Following the aerobic exercise protocol, participants provided a 5 ml sample of peripheral venous blood. In addition, they also completed the same questionnaire and rating scales that they submitted prior to the intervention.

Study instruments included the following:

- Profile of mood states (POMS) [10], a 28-item questionnaire in which participants are asked to report their mood on a 0 (not at all) to 4 (very much) Likert-type scale. This scale was completed twice, once before and again after physical activity. The POMS is composed of five factors reflecting different mood aspects: one positive (vigor-activity) and four negative (fatigue, tension, depression, anger). The items of each factor were summed. In the vigor-activity factor, a higher score reflects a better mood while in the other four factors higher scores indicate a worse mood. The reliability of POMS items was calculated and found to be high, with Cronbach's alpha scores of 0.89 and 0.84. Test–retest reliability of the total POMS score was $r = 0.87$.
- Visual Analogue Mood Scale (VAS) [11], a single-item assessment of affective states indicating current mood. This questionnaire was completed before and after physical activity, with a higher score reflecting a better mood. Following the exercise regimen, mood change was rated on a -3 to +3 scale, where positive scores indicated better mood and negative score signified worse mood, compared to the baseline rating [12].
- World Health Organization Well-being Index (WHO-5), a 5-item instrument to assess well-being. Each item is evaluated on a 0 (never) to 5 (all the time) Likert-type scale [13,14]. Well-being was assessed at baseline.

To neutralize the potential effect of stress on subjects during the study, given the nature of the strenuous exercise regimen, in addition to blood levels of DHEA, we analyzed the ratio of DHEA to cortisol. Analysis of this ratio, rather than just the measurement of DHEA, reflects the level of DHEA controlled for the effects of stress. Thus, the ratio provides a more accurate measure of the effects of increased DHEA levels as a result of physical exercise. Peripheral blood serum levels of DHEA and cortisol were taken immediately before and immediately after physical activity. Samples were collected between the hours of 9:00 and 11:00 in the morning to minimize changes due to circadian variation [5]. A cortisol:DHEA ratio was calculated before exercise and again after exercise. Percent change in hormone levels were calculated pre- and post-exercise. Thus, percent change > 100 indicates an increase of hormone levels in peripheral blood while scores < 100 indicate a decrease.

DHEA levels were determined using recombinant human tumor necrosis factor (TNF)-α enzyme-linked immunosorbent assays (ELISA) kits (IBL international, Hamburg, Germany). Assays were tested following manufacture instructions. The assay used neurosteroid standard capture and detection biotinylated antibodies and streptavidin-horseradish peroxidase. Color intensity induced by the enzymatic reaction was inversely proportional to the concentration of the neurosteroid. Results were determined by reading a sample in an ELISA reader set to 450 nm (BIO-TEK Instruments Inc, Vermont USA).

The associations between background data and treatment group were tested using chi-square tests and grouped *t*-tests, as appropriate according to the nature of the variables. Baseline measures were compared between younger and older subjects using grouped *t*-tests.

Correlation analysis between the change of blood measures and the change of clinical scales were performed using Pearson's correlation coefficient. Two-tailed statistics were used throughout, and $P < 0.05$ was considered significant. Statistical analyses were performed using Statistical Package for the Social Sciences software version 16 (SPSS Inc., Chicago, IL, USA).

## RESULTS

The study comprised 60 subjects, 19 females (31.7%) and 41 males (68.3%), with a mean age of 56.7 ± 17.8 years (range 29–87 years). The demographics of the 60 subjects included 29 who were 50 years of age or younger (mean 39.3 ± 5.4 years, range 29–50 years) and 31 who were older than age 65 (mean 72.8 ± 5.6, range 66–87 years). The proportion of males to females did not differ in the age groups (62% of males were ≤ 50; 74% of males were > 65).

Analysis of hormone levels indicated an increase of DHEA following exercise, while no change in cortisol or the ratio of cortisol:DHEA was found [Table 1]. Paired *t*-tests indicated a significant difference ($P = 0.016$) with regard to DHEA. These measures reflect an increase of 84% in DHEA levels, and 24% of the cortisol:DHEA ratio following exercise. Changes in hormonal levels and mood indicated a significant difference between males and females with regard to cortisol change only. In males, a post-exercise increase of 12% was seen, whereas in females a decrease of 20% ($P = 0.006$) was noted.

Hormone levels were compared between younger and older participants. Lower DHEA levels were measured among younger (3.9 ± 2.6 nmol/L) compared to older (6.5 ± 4.7 nmol/L) participants pre-exercise, while no post-exercise difference was seen (younger 7.4 ± 6.0 nmol/L; older 6.6 ± 5.5 nmol/L). A grouped *t*-test indicated a significant difference on pre-exercise DHEA levels ($P = 0.013$). Percent change of DHEA levels were greater among younger compared to older participants, while cortisol levels hardly changed in either groups [Table 2]. This result was reflected in a reduced cortisol:DHEA ratio among younger subjects, with an increase among older participants. Grouped *t*-tests indicated significant differences of the percentage of DHEA change ($P = 0.02$) and cortisol:DHEA ratio ($P = 0.003$).

According to the five POMS factors, there was a reduction of all negative mood aspects following exercise, with a relatively smaller change in the vigor factor [Table 3]. Paired *t*-tests performed on POMS factors pre- and post-exercise indicated significant reduction of fatigue ($P = 0.004$), tension ($P < 0.001$), depression ($P = 0.011$), and anger ($P = 0.002$), as well as a tendency to significant increase of vigor ($P = 0.08$).

No differences in POMS scores were indicated between younger and older participants pre- and post-exercise.

**Table 1.** Hormone levels pre- and post-physical activity in the entire sample

| | Number of participants | Mean | Standard deviation | *t* | Degrees of freedom | *P* |
|---|---|---|---|---|---|---|
| **DHEA levels*** | | | | | | |
| Pre-exercise | 59 | 5.24 | 4.019 | -2.475 | 58 | 0.016 |
| Post-exercise | 59 | 6.98 | 5.692 | | | |
| **Cortisol** | | | | | | |
| Pre-exercise | 60 | 87.64 | 28.91 | 1.037 | 58 | 0.304 |
| Post-exercise | 60 | 83.84 | 29.15 | | | |
| **Ratio of cortisol:DHEA*** | | | | | | |
| Pre-exercise | 59 | 31.14 | 30.89 | 0.460 | 58 | 0.647 |
| Post-exercise | 59 | 28.61 | 41.36 | | | |

*Data is missing for one sample due to a technical issue in measurement
DHEA = dehydroepiandrosterone

**Table 2.** Change in hormone levels post-exercise comparing young and elderly samples

| | ≤ 50 years of age n=29 | | > 65 years of age n=30 | | | | |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | *t* | Degrees of freedom | *P* |
| DHEA, % change | 236.80 | 186.17 | 133.87 | 142.64 | 2.38 | 57 | 0.02 |
| Cortisol, % change | 103.42 | 43.39 | 99.98 | 44.74 | 0.302 | 58 | 0.764 |
| Cortisol:DHEA, % change | 68.18 | 56.59 | 178.94 | 181.49 | -3.14 | 57 | 0.003 |

Percent change > 100 indicates an increase in peripheral blood levels, whereas scores < 100 indicate a decrease
DHEA = dehydroepiandrosterone, SD = standard deviation

**Table 3.** Comparison of POMS factor before and after exercise in entire sample

| POMS factors | Pre-exercise n=60 | | Post-exercise n=60 | | | | |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | *t* | Degrees of freedom | *P* |
| Vigor | 16.38 | 6.47 | 17.31 | 6.25 | -1.76 | 59 | 0.083 |
| Fatigue | 4.18 | 3.88 | 3.10 | 3.66 | 2.95 | 59 | 0.004 |
| Tension | 1.38 | 1.78 | 0.70 | 1.60 | 4.00 | 59 | 0.001 |
| Depression | 2.15 | 4.05 | 1.60 | 3.34 | 2.61 | 59 | 0.011 |
| Anger | 2.16 | 3.39 | 1.13 | 2.15 | 3.31 | 59 | 0.002 |

POMS = profile of mood states, SD = standard deviation

Similarly, no differences in POMS scores following exercise were indicated. Mood according to VAS, as well as mood change following exercise, did not differ between younger and older participants.

Associations between hormone levels and mood were calculated using Pearson's correlation. No significant associations were indicated before exercise. A significant negative correlation was seen between cortisol and vigor post-exercise ($r = -0.26$, $P = 0.042$). Significant associations were found between change of hormone levels and change of mood: DHEA and VAS ($r = 0.36$, $P = 0.006$), cortisol and fatigue ($r = 0.49$, $P = 0.001$), and cortisol:DHEA ratio and fatigue ($r = 0.32$, $P = 0.031$). No significant associations between baseline well-being and mood change were found.

The associations between changes in hormone levels and changes in mood were calculated separately for younger and older participants. Significant associations were present in older but not younger participants: DHEA change and VAS change ($r = 0.38$, $P = 0.04$), cortisol and fatigue ($r = 0.74$, $P < 0.001$), and cortisol:DHEA ratio and fatigue ($r = 0.59$, $P = 0.02$).

The associations between change of hormone levels and change of mood were calculated separately among males and females. The significant associations reported were present among males only: DHEA change and VAS change ($r = 0.35$, $P = 0.027$), cortisol and fatigue ($r = 0.49$, $P = 0.007$), and cortisol:DHEA ratio and fatigue ($r = 0.46$, $P = 0.03$). The correlation analysis was further performed in gender by age groups, indicating that the associations were present among the older male group: DHEA change and VAS change ($r = 0.31$, $P = 0.15$), cortisol and fatigue ($r = 0.76$, $P < 0.001$), and cortisol:DHEA ratio and fatigue ($r = 0.56$, $P = 0.075$). Due to the smaller sample number ranging from 11–23 participants, results are less significant with only a tendency to significance in two parameters, and only one was significant.

## DISCUSSION

Study results confirm the elevation of DHEA blood levels following aerobic exercise. In addition, to the best of our knowledge, for the first time, study observations indicated an association between elevation in DHEA blood levels and improvement in mood after physical exercise. This association was noted most prominently among the older subjects. As expected, following the exercise protocol, we noted a corresponding enhancement of mood, with a reduction in levels of fatigue, tension, depression, and anger.

Blood levels of DHEA pre- and post-exercise indicated a greater percentage change among the younger subjects than among the older group. Our observations support previous findings indicating lower levels of DHEA with exercise in older populations [5,15]. This result is not surprising because the ability to produce neurosteroids of the DHEA subtype is markedly reduced with age [16]. Thus, while speculative, the observation that the association between improvement in mood following exercise was more prominent in the older group may be explained by the principle of sensitization [17]. Sensitization is a well known concept in physiology whereby individuals respond in a more meaningful and dramatic manner at any small change in baseline low levels of any potential stimulus [17]. Thus, when an individual has no exposure, or very low levels of exposure, to a medication or physiological substance such as a hormone, even low levels or slight increases will lead to an exaggerated physiological response mechanism. This physiological response would thus be potentially greater than even higher levels of exposure to the same substance in those with much higher baseline levels of the material. Since older people have much lower baseline levels of DHEA, those with a demonstrated increase of DHEA levels following exercise, albeit small, might be more sensitized to the well-known positive mood influences and effects of DHEA. The younger subjects have higher baseline levels of DHEA and thus do not respond to the same extent that older populations do in terms of mood and well-being. To obtain significant effects of DHEA on mood post-exercise in the younger population, it may be speculated that much a greater increase in the level of DHEA is required.

While speculative, this hypothesis is suppoprted by the observation that the association of increased DHEA with mood was observed particularly among the older males. This finding may be due to the fact that the drop in levels of DHEA with age is most prominent among males since their levels are much higher than females in their younger years. Thus, compared to elderly females, older males are more sensitized to the effects of an increase in DHEA post-exercise since their levels drop more precipitously as they age. It should be emphasized that the increase in mood following exercise and its relationship to DHEA noted particularly among older males strengthens the observation that exogenous DHEA administration and its improvement in mood and other aspects of the aging process is noted especially among older males [18]. Interestingly, with regard to stress, it has similarly been shown that elderly individuals with higher stress levels who do not participate in aerobic exercise exhibit a significantly higher cortisol:DHEA ratio and flatter DHEA diurnal rhythm levels compared to those who regularly participate in aerobic exercise [19]. We found a similar response following exercise with respect to mood and DHEA levels.

Findings from this study support the prior reports in the literature indicating that DHEA has value in improving well-being in the elderly [16]. Most important, our study findings, while preliminary, seem to indicate that the improvement in mood after exercise is associated with increased DHEA levels. Study observations suggest that, in general, mood elevation following aerobic exercise may be associated with the observed mechanism of increase of DHEA following aerobic exercise.

In this study, we found that the change in DHEA levels is associated with a change in POMS scores. Interestingly, in a study investigating the most prevalent theory regarding runner's high (the beta-endorphin hypothesis), changes in endorphin levels were not shown to be similarly associated with improvement in POMS scores after exercise [20]. While speculative, our results may be supported by studies indicating improvement of mood in a range of ages, not only older individuals, as well as an association of mood with blood levels of DHEA and an improvement of mood following DHEA administration in a variety of subpopulations [21].

In addition to blood levels of DHEA, we analyzed the ratio of DHEA to cortisol to control for the effects of stress. We observed a positive correlation between change in cortisol levels and energy and a negative correlation between cortisol level and fatigue. These findings support previous evidence indicating a similar association between stress and cortisol levels under similar conditions [22].

While current conceptualizations of the phenomenon of runner's high has been hypothesized to be mediated via the opiate, or endocannabinoid, system evidence remains partial and relatively weak. Results of this study indicate that the endogenous neurosteroid system may play a role via DHEA. While speculative, based on the growing body of research in the area of DHEA and depression, it may be hypothesized that DHEA's contribution to runner's high may be mediated by its action on glutamate, σ-1 receptors, catecholamines, neurogenesis, neuroprotection, anti-glucocorticoid, anti-inflammatory, and anti-oxidant properties [21]. As a more long-term result, DHEA may improve mood by its affect on neuronal survival, neurite outgrowth, and neurogenesis [23] as well as neuronal plasticity in the hippocampus, which has been hypothesized to be related to improvement of depressive symptoms [24].

Although observations are interesting, further studies are needed that include larger sample sizes and other sub-populations such as children and professional athletes. In addition, studies are needed that include smaller age ranges of younger individuals and that control for VO2 max, body mass index, contraception use, and levels of physical fitness.

In this study, blood levels of DHEA were obtained immediately after the exercise. Future studies should consider measuring blood levels some time after the exercise to ascertain whether the association between mood change after exercise and DHEA levels is also time related. Since it has been shown that non-athletes increase DHEA levels more than athletes at lower exercise intensities [25], it would be interesting to compare any differences in the effect of DHEA on post-exercise mood between these two subgroups. Finally, regression analysis could provide a suitable model to account for cross-correlations in such a study. However, due to the relatively small number of participants in our study, we opted to present the results in terms of simple rather than multiple associations.

## CONCLUSIONS

Our study supports a relationship between increase in DHEA blood levels after exercise and improvement in mood. This phenomenon appears to be most prominent among older males. These observations, while preliminary, provide an additional consideration in the understanding of the subjective improvement of mood following exercise. Understanding the biological mechanisms of exercise-induced mood changes is critical to the implementation of exercise as a treatment for mood disorders.

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