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The effect of intensive physical training on hormonal regulation and the menstrual cycle in women: metabolic, functional and clinical implications.

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Abstract

The menstrual cycle is one of the most neuroendocrine controlled processes closely involved with the body's response to exercise and metabolism regulation. Menstrual problems and hypothalamic-pituitary-gonadal (HPG) axis dysfunction are linked to increased exercise intensity in women.

The purpose of this study was to examine the impact of physical exercise on hormone control in women and secondary alterations in the menstrual cycle, with particular emphasis on molecular mechanisms, metabolic repercussions, and clinical implications.

A literature review was conducted covering experimental and observational studies on physically active women, including intervention studies (HIIT), population-based studies, analyses of high-intensity training such as military training, and data on hormonal contraception use.Hepcidin concentrations are elevated and iron bioavailability is reduced when the HPA axis is activated and inflammatory mediators are increased in response to exercise. Overt training load suppress GnRH, thus reduce LH, FSH and sex steroids, specifically in the low energy availability state. Among population-based studies, up to 86% women experienced menstrual disorders when subjected to heavy training load. Hormonal contraceptives may prevent variability in the hormonal milieu, but they may cover a HPG axis dysfunction. The menstrual cycle may be less susceptible to training load than to the energetic status and the neuroendocrine response. Amenorrhoea and other menstrual dysfunction are indicators of clinical importance for metabolic abnormality, and there is the need for a tailored training prescription and treatment.

Keywords: menstrual cycle; hypothalamic–pituitary–gonadal axis; RED-S; hepcidin; hormonal contraception; physical training

1. Introduction

The menstrual cycle is a sensitive indicator of a woman's metabolic and energy status. Its proper functioning depends on the continuous pulsatile activity of the hypothalamic–pituitary–gonadal (HPG) axis, which is susceptible to disruption caused by chronic physical stress and energy deficiency. The growing popularity of competitive and recreational sport among women has meant that training-related menstrual disorders are becoming an increasingly common clinical problem, often underdiagnosed and untreated. [2,3,12,13,18,19,25,26]

Epidemiological evidence suggests that menstrual abnormalities can range from as few as some percent to more than 80% of female athletes, depending on the sport and the training load. A particularly important contributing factor for the development of menstrual disturbances appears to be low energy availability (LEA) in the pathogenesis of menstrual disorders, a state in which energy availability is lower than energy cost. In this context the term Relative Energy Deficiency in sport (RED-S) summarizes the hormonal consequences.[10,12,26]

The aim of this study is to evaluate the influence of exercise training on HPG axis regulation and downstream changes of the menstrual cycle, with emphasis on molecular mechanisms, metabolic impact and clinical manifestations. Further we try to determine the impact of hormonal contraceptives on menstrual disturbances.[4,7,8,14]

2. Exercise as an endocrine stimulus — molecular and physiological mechanisms

The Hypothalamic-Pituitary-Adrenal Axis is stimulated with both Endurance and interval training which promotes increased Cortisol release. Acting directly on the Hypothalamus, Cortisol's catabolic action will cause a decrease in pulsatile GnRH release which in turn decreases LH and FSH release.[1,24] Skeletal muscles simultaneously release myokines and particularly Interleukin-6(IL-6) which in a protocol of 8x3 minute high-intensity intervals at 85% of the maximal aerobic speed, showed an increase in IL-6 which in turn stimulated hepcidin production in the hepatocytes (Alfaro-Magallanes et al.) 21 trained female athletes with regular cycles participated in this study and hepcidin is a key regulator of iron homeostasis, being responsible for decreasing the amount of iron released into the blood circulation through internalization of ferroportin. In the female athlete population this leads to a propensity for functional iron deficiency particularly in the early follicular phase when baseline ferritin and serum iron concentrations are already reduced.[1,24,29]

Table 1. The hormonal response to physical exercise — molecular mechanisms and clinical implications [1,14,24]

Axis / mediator	**Change during exercise**	**Molecular mechanism**	**Clinical implications**
HPA (cortisol)	Increase	CRH activation → ACTH → cortisol	GnRH suppression, muscle protein catabolism
Interleukin-6 (myokine)	Increase	produced by skeletal muscles during exercise	induction of hepcidin in hepatocytes
Hepcidin	increase (peaking ~3 hours after exercise)	ferroportin degradation	reduced bioavailability of iron
GnRH	decrease (chronic)	inhibition by cortisol and LEA	ovulation disturbances, irregular periods
LH / FSH	Decrease	absence of pulsatile GnRH secretion	absence of an ovulatory cycle, decrease in oestradiol

This HPA/HPG interaction represents a multilayered regulation where physical activity triggers an inflammatory and stress-mediated regulation of gonadotropin releasing hormone and sex steroids. The final effect is dictated by energy balance and modulating variables like hormonal contraception which may blunt or "steady" the hormonal fluctuations. [5,12,17,18,25,27,28]

3. Clinical trials — specific populations and results

One of the papers investigating the effect of heavy training on menstrual cycles is by Bozzini et al., published in 2023 in Medicine & Science in Sports & Exercise. This research followed 449 women undertaking an 8-week Basic Combat Training course in the U.S. Army and monitored their menstrual cycles, weight and composition and level of activity.They categorised women into different groups dependent upon their regularity of menstrual cycle at the start of training. The findings were unambiguous: the disorders of menstrual cycle, of which the most common were amenorrhoea, irregularities and deviations of duration of cycle were observed up to 86% of patients. The lack of correlation between these disorders and alterations in weight may be of interest since this indicates that the pathophyisiological mechanism includes the involvement of both stress and energy components.

Further population-based data are provided by a 2022 study by Ekenros et al., conducted on a group of 1,086 female athletes representing 57 sports disciplines. Dysmenorrhoea was suffered by 74% of the subjects and premenstrual syndrome symptoms were recorded in 78% of the ladies. The ladies all stated that their aerobic fitness, muscle strength, concentration and quality of sleep was compromised by the different stage of the cycle. A concern remains that despite having obvious symptoms, 18% only thought about the stage of their cycle in planning their training schedule. It seems there is still a significant gap between medical fact and the reality of sport participation. [5,10,28]

Table 2. Summary of selected clinical trials [1,5,9,11]

Study	Population	n	Action / method	Key results
Bozzini et al. 2023	Women in the BCT (US Army)	449	8 weeks of intensive training	86% of participants experienced menstrual cycle irregularities
Alfaro-Magallanes et al. 2022	trained female athletes	21	running intervals (8×3 mins, 85% of maximum heart rate)	increased levels of IL-6 and hepcidin; reduced iron bioavailability

Study	Population	n	Action / method	Key results
Ekenros et al. 2022	female athletes, 57 disciplines	1086	questionnaire survey	74% for dysmenorrhoea, 78% for PMS; only 18% took their cycle into account in their training
Chavan et al. 2024	active women	23	HIIT workout	phase-specific changes in motivation, mood and perceived exertion

4. The effect of hormones on body composition and muscular adaptations

Chronic HPG axis disorders have a multifaceted effect on muscle tissue, regardless of the type of stimulus that triggered them. A decrease in oestradiol concentration limits the activity of mTOR-dependent anabolic pathways and impairs the function of skeletal muscle satellite cells, which play a key role in regeneration and post-workout adaptation processes. The accompanying rise in cortisol enhances proteolytic activity via the ubiquitin–proteasome system, which, under conditions of chronic energy deficiency, can lead to significant muscle mass loss, prolonged recovery times and an increased risk of tissue overload. [6,21,23,30,31]

Additionally, leptin and ghrelin levels are influenced by hormonal changes which can manifest as unexpected alterations in body composition. In some female athletes exhibiting impaired HPG axis activity, chronic energy deficit induced a shift towards adipose tissue accumulation in the trunk combined with loss of muscle mass, likely due to compensatory metabolic alterations. Such alterations defy intuitive perception that exhaustive exercise invariably favorably alters body composition and emphasizes the importance of analyzing hormones to interpret anthropometric alterations in exercising females. [12,22,32]

Table 3. Muscular adaptations and hormones — signalling pathways and clinical effects [1,6,21,23,31]

Hormone	Signalling pathway	Effect on muscle tissue
Oestradiol	mTOR, IGF-1	stimulation of protein synthesis, support for muscle satellite cells; protective effect on muscle and bone tissue

Hormone	Signalling pathway	Effect on muscle tissue
Cortisol	the ubiquitin–proteasome system	increased muscle protein catabolism, inhibition of anabolic processes
ProgesteronProgesterone	the mechanism is unclear	possible inhibitory effect on protein synthesis; inconclusive data
IL-6 (miokina)	AMPK	metabolic changes, modulation of insulin sensitivity, hepcidin induction

5. The effect of hormonal contraception on training response and menstrual cycle regulation

The physiology of the menstrual cycle in physically active women is significantly influenced by the use of hormonal contraceptives; nevertheless, the research has not yet definitively proven how HC affects training adaptations and endocrine system function. A study by Ekenros et al. showed that 63% of 1,086 female athletes used hormonal contraception, and 40% of them reported adverse effects associated with its use. In the group using HC, no significant differences in perceived physical performance were observed depending on the phase of the hormonal cycle, with the exception of the placebo pill period, which was associated with a deterioration in well-being and a reduction in functional parameters. [5,17,28]

Exogenous hormone administration leads to relative stabilisation of the endocrine environment through suppression of the HPG axis, eliminating the physiological fluctuations in oestradiol and progesterone. This reduces the functional variability observed during the different phases of the cycle, but comes at the expense of physiological hormonal regulation. From a mechanistic perspective, chronic GnRH suppression and the absence of ovulation maintain relatively constant but non-physiological concentrations of sex steroids. This may influence the expression of oestrogen receptors in skeletal muscle, the regulation of mTOR- and IGF-1-dependent anabolic processes, and the metabolic response to physical exercise. [6,17,27,31]

A particularly important clinical aspect is the possibility that HC may mask energy and hormonal disturbances, such as secondary amenorrhoea associated with low energy availability. Regular withdrawal bleeding does not necessarily indicate normal HPG axis function and does not rule out coexisting RED-S, which may lead to an underestimation of metabolic problems in female athletes. The absence of physiological oestradiol peaks may, in turn, limit its protective effect on muscle tissue and the skeletal system, which is of particular significance in the context of long-term training adaptation.[6,21,27]

5.1 Clinical comparison — a translational perspective

To illustrate the distinction between the two different hormonal regulation models, the following two theoretical-but real world-cases are presented regarding physically active female patients.

Case I involves a 26-year old female endurance trained athlete with regular eumenorrheic menstrual cycles. She reports variation in performance according to her menstrual cycle, where the early follicular phase is associated with both subjectively increased fatigue and poor performance (coinciding with lower parameters for iron metabolism) and increased fatigue and reduced performance during endurance exercise, with improved performance and subjective exercise tolerance during the late follicular phase. [1,24,29]

The second patient, of a similar age and fitness level, uses combined hormonal contraception. She does not experience cyclical changes in performance or marked differences in her perception of exertion throughout the month. However, during the pill-free interval, she reports a deterioration in her well-being and a reduction in her training capacity, which was also noted in the study by Ekenros et al. From a clinical perspective, the key difference between these patients is not their fitness levels per se, but their ability to identify potential disorders. In the first patient, changes in the menstrual cycle may constitute an early marker of metabolic dysfunction, whereas in the second, regular withdrawal bleeding may mask this dysfunction. [5,17,27,28]

Table 4. Comparison of hormonal and training parameters — natural cycle vs hormonal contraception [5,12,17,18,28,29]

Parameter	Workout + natural cycle	Workout + hormonal contraception
HPG axis	active, physiological	suppression
GnRH	pulsatile secretion	inhibited

Parameter	Workout + natural cycle	Workout + hormonal contraception
Oestradiol	dynamic phase fluctuations	stable, below the physiological range
Progesterone	Present luteal phase	none
Ovulation	Present	none
Variability in performance	present (phase)	minimalnaminimum
Perception of exertion	variable during the cycle	more stable
Training adaptation	physiological, phase-dependent	potentially flattened
Diagnosis of impairments	possible (e.g. secondary amenorrhoea)	difficult
The risk of masking RED-S	low	high
A period of reduced physical form	no clear pattern	pill-free interval

6. Discussion

The data collected confirm that physical training acts as a powerful modulator of the female endocrine system, affecting both physical performance and reproductive function. A key observation arising from the analysed studies, however, is that the determining factor for menstrual disorders is not the intensity of exercise itself, but the metabolic context, primarily energy availability and the body's ability to adapt to chronic physical stress. The findings of the study by Bozzini et al. provide particularly compelling evidence in this regard: an 86% prevalence of menstrual cycle disorders among women undergoing intensive military training, with no correlation to weight loss, suggests a pathogenesis that goes beyond simple energy balance. The changes in body weight do not appear to be a valid clinical indicator – a low energy supply can be maintained with or without a substantial loss in weight, which cannot be easily diagnosed in a non- specialist clinical setting or by laboratory testing without specialist assessment. [10,13,15,19]

The increase in hepcidin levels following intense exercise, resulting from stimulation by IL-6, limits iron bioavailability in a manner that is cyclically dependent on the menstrual phase. This mechanism may partly explain why performance impairments in female athletes often precede the onset of overt anaemia and do not correlate with classic blood count parameters. Assessment of ferritin and hepcidin levels should therefore be a standard part of the diagnostic workup in physically active women with symptoms of unexplained fatigue or reduced exercise capacity. [1,16]

Prospective studies are needed to further examine the long-term effects of hormonal contraception on training adaption. Although there is conflicting evidence, the anabolic and protective effects of oestradiol on muscle and bone tissue may be limited by the suppression of physiological oestradiol peaks. The predominance of cross-sectional and survey research over randomized controlled trials is a major drawback of the literature currently accessible, making it challenging to draw definitive cause-and-effect conclusions. Prospective studies with long-term follow-up are still desperately needed to evaluate the effects of HC on training adaptations as well as the clinical ramifications of persistent masking of HPG axis dysfunction. [6,24,27]

7. Clinical implications

The assessment of physically active women should routinely include an analysis of HPG axis function and energy availability, rather than focusing solely on performance parameters. Menstrual cycle disorders, including secondary amenorrhoea or a shortened luteal phase, should be treated as an early marker of metabolic dysfunction and potential RED-S, requiring diagnosis and intervention - rather than being dismissed as an inevitable side effect of sport. [12,18,25]

Women using hormonal contraception should be monitored more closely. Frequent withdrawal bleeding does not rule out concurrent hormonal problems and does not represent the physiological activity of the HPG axis. Clinical symptoms, recovery quality, energy levels, and laboratory parameters—particularly iron metabolism and metabolic markers—must all be evaluated in this group. [17,27]

The approach should be interdisciplinary, encompassing the personalisation of training loads, the optimisation of energy availability and — where appropriate — consultation with an endocrinologist or gynaecologist. The integration of knowledge in the fields of exercise physiology, reproductive endocrinology and sports medicine is essential for the effective and safe care of physically active women. [12,18,25]

8. Conclusions

Physical training powerfully influences the hypothalamic-pituitary-gonadal axis but the underlying determinants of menstrual cycle abnormalities are not exercise intensity but rather energy availability and activation of the stress axis chronically. Increased levels of cortisol and inflammatory mediators, such as IL-6, causes downstream inhibition of GnRH resulting in subsequent decrease in LH, FSH, and sex steroids.The greatest clinical significance is observed in relation to iron metabolism and psychophysiological responses. The impact of the menstrual cycle phases on strength adaptations remains limited, whereas performance impairments in women are more often due to central and metabolic factors than to muscular limitations. Low energy status, in the absence of any significant body weight changes, could also result in disturbances of menstrual function that may not be readily detectable by standard methods on clinical examination. [1,13,19,23]

Administration of hormonal contraceptive medication can cover up the signs of HPG axis dysregulation, hence obscuring its timely diagnosis and treatment. Overall, a woman’s response to training should be viewed as the result of a dynamic balance between exercise, recovery and hormonal regulation, which underscores the need for individualisation of both the training and clinical approaches. [17,20,27]

9. Summary

The physiology of a woman who exercises is a dynamic system in which the balance between anabolic and catabolic hormonal signals determines the ultimate outcome of training. A disruption of this balance leads not only to a decline in performance, but also to clinically significant health consequences that extend beyond the reproductive sphere.

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