

The Functional Hypothalamic Amenorrhea in Adolescents and Young Women

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Abstract: Functional hypothalamic amenorrhea (FHA) is a prevalent yet understudied neuroendocrine disorder affecting adolescents and young women, particularly female athletes and individuals with eating disorders. Societal pressures promoting extreme leanness and intense athletic performance exacerbate FHA risks, yet research on tailored interventions remains limited. This meta-analysis synthesizes current evidence on FHA's etiology, focusing on its dual triggers—psychological stress and energy deficiency—and evaluates multidisciplinary management strategies. The study aims to consolidate existing knowledge, identify gaps in care, and propose targeted solutions for high-risk populations. By analyzing five key studies, the paper reveals that FHA arises from hypothalamic-pituitary-ovarian axis suppression due to elevated cortisol, leptin deficiency, and disrupted kisspeptin signaling. Effective treatment requires integrated approaches: cognitive-behavioral therapy for stress reduction, nutritional rehabilitation for energy repletion, and exercise modification for athletes. The findings underscore the urgency of early intervention to prevent bone loss, cardiovascular risks, and infertility. Future research should prioritize randomized trials to validate personalized protocols and explore sociocultural influences on FHA development.

Keywords: Functional hypothalamic amenorrhea, Female athletes, Eating disorders, Neuroendocrine disruption

1. Introduction

Functional hypothalamic amenorrhea (FHA) is a neuroendocrine disorder causing missed periods for more than 3 months without anatomical abnormalities [1]. It differs from other amenorrhea types because it results from disrupted hormone signaling due to low energy intake, intense exercise, or chronic stress [2]. Young women, particularly athletes and those with eating disorders, are disproportionately affected [3]. FHA often goes undiagnosed in high-risk groups despite serious health risks. Prolonged FHA weakens bones (increasing fracture risk), disrupts cardiovascular health, and raises infertility risks [1]. Societal pressures to be thin or athletic worsen the problem, yet few studies address prevention or tailored treatments for vulnerable populations [2].

This essay highlights why FHA demands urgent attention. Many sufferers dismiss missed periods as "normal," delaying care until complications arise. To clarify gaps in knowledge, this meta-analysis synthesizes five key studies, examining the causes of FHA and current treatments. The goal is to push for better treatment for FHA and targeted treatment, especially for athletes and eating disorder patients. By consolidating current evidence, this work also provides a roadmap for future research to reduce FHA's burden.

2. Etiology and pathophysiology: neuroendocrine disruption in FHA

Functional Hypothalamic Amenorrhea (FHA) is characterized by hypothalamic dysregulation, leading to suppressed gonadotropin-releasing hormone (GnRH) pulsatility and subsequent disruption of the hypothalamic-pituitary-ovarian (HPO) axis. This dysregulation arises from a combination of metabolic, psychological, and nutritional stressors, which alter neuroendocrine signaling. Key mechanisms include elevated cortisol levels due to chronic stress, which inhibit GnRH secretion, and reduced leptin levels from low energy availability, further impairing hypothalamic function [2]. Additionally, disruptions in kisspeptin signaling, a critical regulator of GnRH neurons, contribute to the suppression of reproductive hormones [4]. These neuroendocrine disturbances result in decreased luteinizing hormone (LH) and follicle-stimulating hormone (FSH) release, ultimately leading to anovulation and amenorrhea. The suppression of the HPO axis in FHA is primarily driven by interrelated triggers, including psychological stress, disordered eating, low body weight, and excessive exercise. These factors often coexist and create a synergistic disruption of neuroendocrine function [2].

2.1. Psychological stress and HPA axis dysregulation

A growing body of evidence identifies psychological stress as a contributor to Functional Hypothalamic Amenorrhea (FHA). The condition develops when sustained stress interferes with neuroendocrine signaling in the hypothalamic-pituitary-ovarian (HPO) axis. Research demonstrates that activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis elevates cortisol concentrations, which in turn dampens the pulsatile secretion of GnRH [5]. This suppression subsequently diminishes LH and FSH production, impairing normal ovarian function. Common stressors ranging from academic demands to interpersonal difficulties frequently preceded FHA onset, with approximately half of affected adolescents reporting clinically significant psychosocial triggers [6]. The stress response also involves γ -aminobutyric acid (GABA), the brain's primary inhibitory neurotransmitter, which when elevated can further suppress GnRH neuronal activity [3]. Beyond menstrual irregularities, these endocrine disturbances increase risks for bone density loss and metabolic dysfunction, highlighting stress reduction as a critical component of therapeutic intervention.

2.2. Energy deficiency and metabolic adaptations

Functional hypothalamic amenorrhea (FHA) fundamentally results from chronic energy deficiency that disrupts hypothalamic-pituitary-ovarian (HPO) axis function. This energy deficit state manifests through three primary pathways: disordered eating, low body weight, and excessive exercise, each contributing to and exacerbating the metabolic imbalance that underlies FHA.

Pathogenesis begins with inadequate energy availability, which triggers a neuroendocrine cascade. When energy intake fails to meet physiological demands, the hypothalamus perceives a starvation state and downregulates non-essential functions, including reproduction [5]. This adaptive response occurs through several mechanisms: decreased leptin secretion from diminished adipose tissue stores, increased cortisol production, and altered ghrelin and peptide YY levels [5]. These metabolic signals converge to suppress kisspeptin neurons in the arcuate nucleus, resulting in reduced GnRH pulsatility and consequent hypoestrogenism [5].

Disordered eating behaviors directly create energy deficiency through chronic caloric restriction, purging, or erratic eating patterns. Even in normal-weight individuals, these behaviors can maintain a state of metabolic stress sufficient to impair GnRH secretion [5]. The resulting hypoleptinemia (<3 ng/mL) fails to provide adequate stimulation to kisspeptin neurons, while elevated cortisol further inhibits reproductive axis activity [4].

Low body weight, particularly when accompanied by rapid weight loss, intensifies this energy deficit. Adipose tissue reduction below critical thresholds (typically <22% body fat) dramatically decreases leptin production, removing a key signal for reproductive function [5]. The resulting metabolic adaptations prioritize essential physiological processes at the expense of reproduction, creating persistent HPO axis suppression.

Excessive exercise compounds energy deficiency by increasing caloric expenditure without adequate compensation. Athletic activities that emphasize leanness or endurance particularly disrupt this balance, as the combination of physical stress and energy deficit amplifies HPO axis suppression [5]. Exercise-induced increases in cortisol and CRH create additional inhibition of GnRH neurons, while sport-specific endocrine adaptations may alter LH/FSH ratios in some athletes [3].

These interconnected pathways indicate that FHA treatment requires comprehensive energy repletion through nutritional rehabilitation, weight restoration, and exercise modification to reestablish normal HPO axis function [5].

3. Clinical management: a multidisciplinary approach to FHA

The management of FHA typically involves a multidisciplinary approach, integrating medical, nutritional, and psychological interventions [1]. The primary goal is to address the underlying causes of the condition, which often include stress, disordered eating, and excessive exercise. A collaborative effort between healthcare providers, dietitians, and mental health professionals is essential to provide comprehensive care and support for affected individuals.

3.1. Stress reduction strategies

Stress is a significant contributor to FHA, and managing it effectively is crucial for recovery. Cognitive-behavioral therapy (CBT) has been shown to be particularly effective in addressing the psychological aspects of FHA. CBT helps individuals identify and challenge negative thought patterns and behaviors that contribute to stress, thereby reducing its impact on the HPO axis [6]. Techniques such as mindfulness meditation, progressive muscle relaxation, and guided imagery can also be beneficial in managing stress levels [2]. Additionally, incorporating stress-reducing activities such as yoga, tai chi, or other forms of gentle exercise can provide both physical and psychological benefits.

3.2. Nutritional rehabilitation and exercise modification

Energy deficiency in FHA can result from low caloric intake and excessive exercise, both of which disrupt the normal functioning of the HPO axis. Addressing these issues requires a tailored approach that considers the specific needs and circumstances of each individual.

Low Caloric Intake

For individuals with FHA resulting from low caloric intake, particularly those with eating disorders, nutritional rehabilitation is paramount. This involves working with a registered dietitian to develop a balanced meal plan that meets the individual's energy needs. The focus is on gradual weight restoration and the normalization of eating patterns to ensure adequate caloric intake [1]. Cognitive-behavioral therapy can also play a crucial role in addressing the psychological aspects of disordered eating, helping individuals develop healthier attitudes towards food and body image [3].

4. Special populations: tailored interventions for female athletes and eating disorder patients

Female athletes are particularly at risk for FHA due to the high energy demands of their training regimens. For these individuals, a balanced approach to exercise is essential. This may involve reducing the intensity or duration of training sessions, incorporating rest days, and ensuring adequate recovery periods [4]. Additionally, athletes should be educated on the importance of proper nutrition to support their energy needs and overall health. In some cases, working with a sports dietitian can help athletes develop a personalized nutrition plan that supports their athletic performance while minimizing the risk of FHA.

Female athletes and individuals with eating disorders often require specialized interventions to address the unique challenges they face. For female athletes, the Female Athlete Triad Coalition recommends a comprehensive approach that includes medical evaluation, nutritional counseling, and psychological support [3]. This approach aims to address the interrelated components of the Female Athlete Triad—energy availability, menstrual function, and bone health—while promoting a healthy and sustainable approach to sports participation.

For individuals with eating disorders, a multidisciplinary team approach is essential. This typically involves collaboration between healthcare providers, dietitians, and mental health professionals to address both the physical and psychological aspects of the disorder [1]. Cognitive-behavioral therapy and family-based therapy have been shown to be effective in treating eating disorders and can be adapted to address the specific needs of individuals with FHA [6].

5. Future directions: bridging gaps in FHA research and care

Future research on Functional Hypothalamic Amenorrhea (FHA) should focus on several critical areas to enhance our understanding and management of this condition, particularly in female athletes. Given the multifactorial nature of FHA, future studies should aim to elucidate the complex interplay between psychological, physiological, and sociocultural factors that contribute to its development and persistence.

5.1. Importance of further study for female athletes

Female athletes are particularly vulnerable to FHA due to the unique demands of their training regimens and the societal pressures they face. The Female Athlete Triad, which includes FHA, low energy availability, and poor bone health, highlights the need for targeted research to address the specific needs of this population [4]. Understanding the mechanisms underlying FHA in female athletes is essential for developing effective prevention and intervention strategies that can enhance their health and performance without compromising their athletic aspirations.

5.2. Sociocultural influences and gender-specific training

Future research should explore the impact of societal expectations on female athletes, particularly the pressure to maintain a lean physique, which can lead to disordered eating and excessive exercise [3]. Additionally, the influence of gender-specific training practices should be examined. While male athletes often focus on strength and power, female athletes may face unique challenges related to body image and energy balance. Investigating the differences in training practices and their impact on FHA can inform the development of gender-specific guidelines and support systems.

Explore the impact of sociocultural factors, such as body image issues and societal pressures, on the development of FHA. Qualitative studies, such as interviews and focus groups, can provide valuable insights into the lived experiences of female athletes and the challenges they face in

balancing athletic performance with health. Surveys and cross-sectional studies can also be used to assess the prevalence of body image concerns and disordered eating behaviors in this population. Understanding the sociocultural factors contributing to FHA can inform the development of targeted interventions and support systems that address the psychological and social aspects of the condition [3].

5.3. Innovations in psychological and nutritional interventions

Intervention Studies should evaluate the efficacy of various interventions, including nutritional counseling, psychological support, and modified training regimens. Randomized controlled trials (RCTs) should be conducted to assess the impact of these interventions on restoring menstrual function and improving overall health outcomes in female athletes with FHA. Interventions should be tailored to address the specific needs of female athletes, such as personalized nutrition plans and stress management techniques.

5.3.1. Gender-specific training practices

Studies should investigate the differences in training practices between male and female athletes and their impact on energy balance and menstrual function. Comparative studies should analyze training regimens, energy expenditure, and dietary intake in male and female athletes. These studies should also assess the prevalence of FHA and related conditions in both populations to identify gender-specific risk factors. Gender-specific training guidelines can help optimize performance while minimizing the risk of FHA and other health issues in female athletes [1].

5.3.2. Psychological interventions

Studies should explore the effectiveness of psychological interventions, such as cognitive-behavioral therapy (CBT), in addressing the psychological aspects of FHA. RCTs should evaluate the impact of CBT and other psychological interventions on stress reduction, disordered eating behaviors, and menstrual health in female athletes. Studies should also investigate the role of mindfulness and other stress-reduction techniques in managing stress and improving mental health. Psychological interventions can help address the underlying stress and disordered eating behaviors that contribute to FHA, improving both mental and physical health outcomes [4].

5.3.3. Nutritional interventions

Develop and evaluate personalized nutrition plans that address the specific energy needs of female athletes. Studies should focus on the development of nutrition plans that optimize energy intake and nutritional balance to support both athletic performance and menstrual health. These plans should be tailored to individual athletes based on their training intensity, body composition, and metabolic needs. Personalized nutrition plans can help female athletes achieve and maintain energy balance, reducing the risk of FHA and improving overall health [1].

6. Conclusion

This paper has examined functional hypothalamic amenorrhea (FHA) as a neuroendocrine disorder driven by stress, energy deficiency, and sociocultural pressures, with a focus on its disproportionate impact on female athletes and individuals with eating disorders. Key findings underscore the need for multidisciplinary interventions—combining psychological support, nutritional rehabilitation, and exercise moderation—to restore menstrual function and mitigate long-term health risks.

While this analysis consolidates current evidence on FHA's etiology and management, it has limitations. The paper does not explore genetic predispositions to FHA in depth, nor does it employ longitudinal studies to assess the efficacy of interventions over time. Additionally, cultural variability in body image pressures and access to care remains underexamined.

Future research should prioritize randomized controlled trials to validate personalized treatment protocols, particularly for high-risk groups. Investigations into the role of gut microbiota in energy metabolism and FHA, as well as the development of digital health tools for early detection, could revolutionize care. By addressing these gaps, the medical community can better safeguard the reproductive and metabolic health of vulnerable populations.

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