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THE IMPACT OF CHRONIC STRESS ON MENSTRUAL DISORDERS IN WOMEN OF REPRODUCTIVE AGE: A LITERATURE REVIEW

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ABSTRACT

Chronic psychological and physical stress is a major contributor to menstrual disturbances in women of reproductive age. This review aims to synthesize current evidence on the mechanisms, clinical implications, and management of stress-related menstrual dysfunction, with particular focus on hypothalamic suppression. Methods included comprehensive evaluation of observational studies, clinical trials, and experimental research addressing neuroendocrine, metabolic, and behavioral pathways affected by prolonged stress, energy deficiency, and intensive physical activity. Findings indicate that chronic stress disrupts hormonal regulation by inhibiting gonadotropin secretion and impairing ovarian function, leading to reduced estrogen production and anovulation. Energy deficiency and excessive physical exertion exacerbate these effects, resulting in prolonged hypoestrogenism, impaired fertility, and decreased bone mineral density. Women affected may present with normal body weight, complicating early detection and diagnosis. Multidisciplinary management strategies, including lifestyle modification, nutritional support, moderated physical activity, and psychological interventions, have been shown to restore menstrual function and mitigate long-term complications. In selected cases, pharmacological interventions may be necessary to preserve bone health and support reproductive outcomes. Overall, stress-induced menstrual disorders result from a complex interplay between psychological, metabolic, and physical factors, requiring individualized assessment and treatment. Early identification and intervention are essential to prevent chronic health consequences, optimize reproductive potential, and maintain overall well-being. The review highlights gaps in understanding of individual susceptibility, recovery timelines, and long-term metabolic and cognitive outcomes, emphasizing the need for further research to develop targeted preventive and therapeutic strategies for women at risk of stress-related menstrual dysfunction.

KEYWORDS

Functional Hypothalamic Amenorrhea, HPO Axis, Energy Deficiency, Fertility, Reproductive Health

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1. Introduction

Chronic stress is increasingly recognized as a significant risk factor for numerous physiological and psychological disturbances, with particular implications for women of reproductive age. One of the most well-documented consequences of prolonged stress exposure is the disruption of normal menstrual function. Among the various stress-related reproductive disorders, **functional hypothalamic amenorrhea (FHA)** constitutes a predominant and extensively studied condition. FHA is typically associated with psychological stress, excessive physical exertion, and inadequate energy availability, and is defined as secondary amenorrhea resulting from reversible hypothalamic dysfunction in the absence of structural abnormalities of the ovaries, pituitary gland, or other components of the reproductive axis (Berga et al., 1989; Laughlin & Yen, review article). This condition reflects a complex interaction between environmental stressors and neuroendocrine regulation, making it a valuable model for studying the physiological consequences of chronic stress.

The **pathophysiology of FHA** is primarily driven by hyperactivation of the hypothalamic–pituitary–adrenal (HPA) axis in response to chronic or cumulative stress. Elevated cortisol levels, which represent a hallmark of prolonged HPA axis activation, exert an inhibitory effect on the pulsatile secretion of gonadotropin-releasing hormone (GnRH) by hypothalamic neurons. This suppression disrupts normal communication within the hypothalamic–pituitary–ovarian (HPO) axis, ultimately impairing ovarian steroidogenesis (Berga et al., 1988; Richards et al., 2000; Schaefer et al., 2018). As a result, reductions in luteinizing hormone (LH) and follicle-stimulating hormone (FSH) secretion contribute to diminished estradiol production and ovarian follicular development. Over time, these endocrine alterations can lead not only to amenorrhea, but also to a broad spectrum of health consequences, including decreased bone mineral density, impaired fertility, metabolic dysregulation, and adverse psychological outcomes (Laughlin & Yen, review article; Gordon et al., 2020/2021).

Epidemiological observations indicate that FHA most frequently affects women between 18 and 35 years of age, particularly those exposed to academic pressure, high-intensity athletic training, or restrictive dietary practices. Importantly, menstrual disturbances associated with stress may occur throughout the entire reproductive lifespan, underscoring the broad susceptibility of women to stress-induced neuroendocrine dysregulation (Gordon et al., 2020/2021; Smith-Rogers et al., 2025). A notable and diagnostically relevant aspect of FHA is that many affected women present with a **normal or even above-average body mass index (BMI)**. Therefore, diagnosis cannot rely solely on anthropometric measures but instead requires a comprehensive assessment of lifestyle factors, nutritional patterns, psychological stress, and behavioral indicators such as excessive exercise or maladaptive coping strategies (Richards et al., 2000; Berga et al., 1989).

Given the complexity and multifactorial nature of FHA, as well as its significant long-term health consequences, a systematic and critical evaluation of the literature is essential. The present review aims to provide an in-depth synthesis of current knowledge regarding the impact of chronic stress on menstrual function in women of reproductive age. Specifically, it examines the underlying neuroendocrine mechanisms, delineates major risk factors, discusses clinical manifestations and health implications, and evaluates contemporary diagnostic and therapeutic approaches. By integrating findings from both foundational and recent studies, this review seeks to identify gaps in existing knowledge, highlight ongoing debates in the field, and propose future directions for research on FHA and related stress-induced menstrual disorders.

2. Pathophysiological Mechanisms

2.1 HPA Axis Activation and HPO Axis Suppression

Chronic psychological and physical stress are well-established triggers of functional hypothalamic amenorrhea (FHA), primarily through the activation of the hypothalamic–pituitary–adrenal (HPA) axis. Sustained stress exposure leads to increased secretion of adrenocorticotropic hormone (ACTH) and cortisol, which in turn exerts inhibitory effects on the hypothalamic–pituitary–ovarian (HPO) axis (Berga et al., 1988; Schaefer et al., 2018; Richards et al., 2000). Women with FHA exhibit exaggerated basal and stress-induced cortisol responses, which contribute to the suppression of pulsatile gonadotropin-releasing hormone (GnRH) secretion. Consequently, this leads to reduced luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels, decreased estrogen production, and menstrual irregularities ranging from oligomenorrhea to complete amenorrhea (Laughlin & Yen, review article; Gordon et al., 2020/2021). As illustrated in Figure 1, chronic stress, energy deficiency, and excessive physical activity converge to suppress GnRH pulsatility, reduce gonadotropin secretion, and lead to hypoestrogenism and its clinical consequences.

Beyond gonadotropin suppression, chronic HPA axis hyperactivation induces complex neuroendocrine alterations involving key regulatory peptides such as kisspeptin, neuropeptide Y, and corticotropin-releasing hormone (CRH). Kisspeptin, a critical stimulator of GnRH neurons, is particularly sensitive to stress and energy availability, and its dysregulation further diminishes GnRH pulsatility (Berga et al., 1989; Barbagallo et al., 2023). These mechanisms highlight the intricate crosstalk between stress-related neuroendocrine pathways and reproductive function, emphasizing that FHA represents a multi-factorial disruption rather than a primary ovarian pathology. Moreover, prolonged hypercortisolemia may have downstream effects on cardiovascular, metabolic, and neurocognitive health, illustrating the systemic impact of chronic stress in women with FHA.

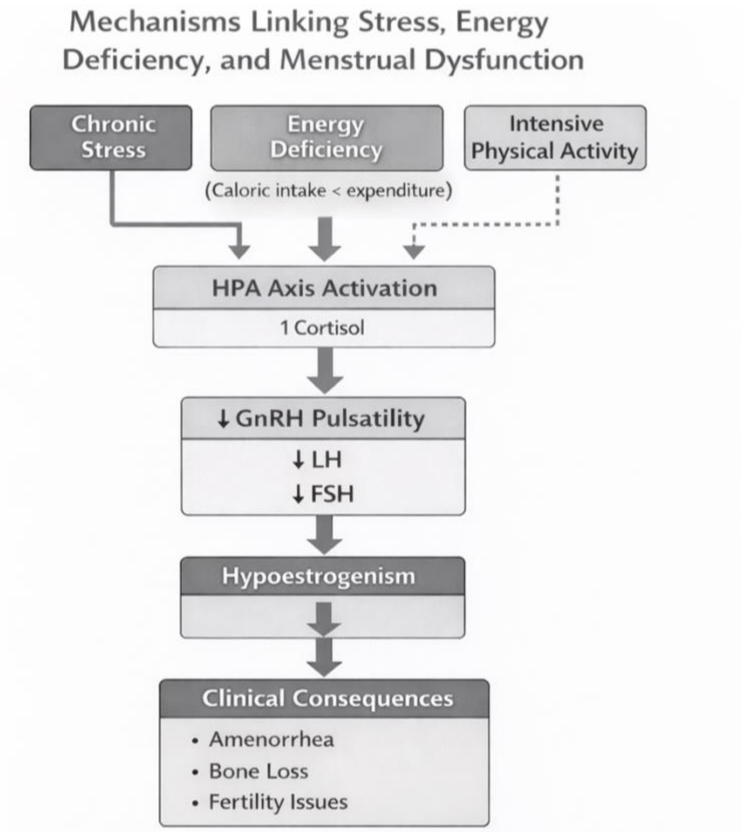

Figure 1. Mechanisms linking chronic stress, energy deficiency, and intensive physical activity to functional hypothalamic amenorrhea. The diagram illustrates the main neuroendocrine and metabolic pathways, showing how these factors activate the HPA axis, reduce GnRH pulsatility, lower LH and FSH secretion, and lead to hypoestrogenism with clinical consequences such as amenorrhea, bone loss, and fertilty issues.

2.2 Energy Deficiency and Intensive Physical Activity

Energy deficiency, defined as a persistent imbalance in which caloric intake fails to meet energy expenditure, is a pivotal factor in the pathogenesis of FHA. Chronic low energy availability suppresses GnRH pulsatility, decreases LH and FSH secretion, reduces estradiol levels, and ultimately disrupts menstrual cyclicity (Berga et al., 1989; Gordon et al., 2020/2021). This is particularly pronounced in athletes engaged in high-intensity or endurance training, aesthetic sports, or activities requiring strict weight regulation. The combination of excessive physical activity and low energy intake amplifies HPA axis activation, further elevating cortisol levels and reinforcing the inhibitory effects on the HPO axis (Schaefer et al., 2018).

The consequences of energy deficiency extend beyond reproductive dysfunction. Chronic hypoestrogenism combined with hypercortisolemia increases the risk of low bone mineral density, osteopenia, and osteoporosis, even in young women (Bikle et al., 2016; Laughlin & Yen, review article). Metabolic alterations, including impaired glucose homeostasis, dyslipidemia, and hormonal imbalances, are also frequently observed. Interventions aimed at restoring energy balance—through tailored nutritional support, moderated exercise, and weight optimization—have been shown to re-establish GnRH pulsatility, normalize menstrual function, and improve long-term reproductive and skeletal outcomes (Smith-Rogers et al., 2025; Barbagallo et al., 2023).

2.3 Psychoneuroendocrine Interactions

FHA exemplifies a disorder in which psychological stress, energy deficiency, and excessive exercise interact within complex psychoneuroendocrine networks. Chronic stress elevates cortisol and other stress mediators, influencing not only reproductive physiology but also neurological health, including cognition, mood regulation, and neuroprotection (Bikle et al., 2016). Psychological stressors such as social pressure, perfectionism, and mood disorders may exacerbate HPA axis hyperactivity, alter eating behavior, and contribute to energy imbalance, creating a vicious cycle that perpetuates menstrual dysfunction (Gordon et al., 2020/2021; Barbagallo et al., 2023).

Current evidence suggests that menstrual irregularities can serve as an early and sensitive marker of chronic stress and neuroendocrine dysregulation. The early identification of FHA allows timely interventions, including nutritional rehabilitation, structured exercise modification, and targeted psychological support, which collectively mitigate the adverse consequences of chronic stress on reproductive, skeletal, and overall health (Smith-Rogers et al., 2025; Laughlin & Yen, review article). Future research is warranted to delineate individual susceptibility factors, such as genetic and epigenetic modulators of HPA and HPO axis responsiveness, to enable personalized preventive and therapeutic strategies for women at risk of FHA.

3. Risk Factors and Epidemiology

Functional hypothalamic amenorrhea (FHA) is a multifactorial disorder resulting from the dynamic interaction of psychological, metabolic, and physical stressors that collectively disrupt the regulatory mechanisms of the hypothalamic–pituitary–ovarian (HPO) axis. Epidemiological evidence demonstrates that disturbances in neuroendocrine signaling pathways are frequently precipitated by chronic stress exposure, states of energy deficiency, excessive physical activity, and alterations in body composition. These factors often coexist, amplifying their individual effects and contributing to the onset and persistence of menstrual dysfunction. A deeper understanding of the prevalence of FHA in various population groups underscores the need for systematic screening and early preventive strategies, particularly among individuals exposed to heightened psychosocial or metabolic demands (Gordon et al., 2020/2021; Laughlin & Yen, review article).

3.1 Chronic Psychological Stress

Chronic psychological stress—including occupational, academic, interpersonal, or trauma-related pressures—remains one of the most prominent and consistently reported risk factors for FHA. Prolonged activation of the hypothalamic–pituitary–adrenal (HPA) axis leads to sustained cortisol elevations, which interfere with the hypothalamic secretion of gonadotropin-releasing hormone (GnRH). This hormonal imbalance suppresses pulsatile luteinizing hormone (LH) and follicle-stimulating hormone (FSH) release, subsequently impairing ovarian steroidogenesis (Berga et al., 1988; Richards et al., 2000; Schaefer et al., 2018).

Moreover, individual differences in stress reactivity—shaped by genetic predisposition, early-life experiences, cultural environment, and coping strategies—modulate the likelihood of menstrual disruption. As a result, some women experience significant reproductive suppression in response to moderate stressors, while others maintain regular cycles despite chronic or intense stress exposure (Bikle et al., 2016; Barbagallo et al., 2023). Longitudinal research further suggests that chronic stress is not limited to reproductive consequences; it can contribute to widespread neuroendocrine dysregulation, affecting metabolic health, bone turnover, sleep quality, and cognitive functioning. Consequently, evaluating psychosocial context and stress biomarkers is essential in the diagnostic workup for menstrual irregularities.

3.2 Energy Deficiency and Eating Behaviors

Energy deficiency—defined as a persistent mismatch between energy intake and expenditure—is one of the most thoroughly investigated mechanisms underlying FHA. Reduced caloric intake, whether intentional through dieting, associated with eating disorders such as anorexia nervosa or bulimia nervosa, or emerging from increased energy demands without compensatory intake, directly impairs GnRH pulsatility and downregulates ovarian hormone production (Smith-Rogers et al., 2025; Gordon et al., 2020/2021).

Beyond reproductive suppression, chronic low energy availability contributes to systemic metabolic adaptations, including alterations in thyroid hormone regulation, reduced leptin and insulin-like growth factor 1 (IGF-1) levels, and diminished bone mineral density. These physiological adjustments prioritize survival over reproductive function, reflecting an adaptive but ultimately detrimental response to perceived starvation. Importantly, epidemiological studies indicate that FHA can occur even in women with a normal or slightly elevated BMI, highlighting that overall energy availability—not body mass alone—is the primary determinant of neuroendocrine disruption. This underscores the need for clinicians to conduct detailed nutritional assessments rather than relying exclusively on anthropometric measures.

3.3 Intensive Physical Activity

High-intensity or high-volume physical activity represents another major precipitating factor for FHA, particularly in athletic populations. Prolonged or strenuous exercise increases metabolic demands and activates the HPA axis, contributing to elevated cortisol levels that antagonize reproductive hormone pathways (Schaefer et al., 2018; Gordon et al., 2020/2021). This risk is especially pronounced in sports emphasizing endurance, low body weight, or aesthetic appearance, such as long-distance running, gymnastics, ballet, and figure skating.

Notably, physical activity alone does not uniformly result in menstrual dysfunction; rather, FHA emerges when intense training occurs in the context of insufficient energy intake or additional psychosocial stressors. Longitudinal data reveal that athletes experiencing chronic energy deficiency exhibit markedly higher rates of oligomenorrhea and amenorrhea. These findings highlight the importance of monitoring exercise load, nutritional adequacy, and menstrual patterns in active women to prevent long-term complications, including stress fractures, hormonal imbalances, and cognitive changes associated with prolonged hypoestrogenism.

3.4 Low BMI and Rapid Weight Loss

Low BMI and rapid, unintentional or intentional weight loss contribute significantly to FHA risk. Even modest decreases in body weight can alter leptin levels, disrupt thyroid function, and heighten HPA axis activity, collectively impairing reproductive hormone secretion (Berga et al., 1989; Richards et al., 2000). Clinical observations indicate that women with fluctuating or chronically low BMI experience disproportionately higher rates of menstrual irregularities compared to those with stable body composition.

Importantly, weight loss–induced FHA may develop insidiously, with menstrual changes emerging only after several months of metabolic instability. Rapid reductions in fat mass are particularly impactful because adipose-derived hormones—such as leptin and adiponectin—play key roles in signaling energy sufficiency to the hypothalamus. Consequently, assessment of body composition changes, rather than weight alone, is essential for identifying individuals at heightened risk.

3.5 Age and Population-Specific Epidemiology

FHA primarily affects women between 18 and 35 years of age, corresponding to life stages characterized by significant academic pressures, career development, and participation in competitive sports (Laughlin & Yen, review article; Gordon et al., 2020/2021). However, the condition can occur across the reproductive lifespan, with prevalence influenced by lifestyle, environmental stressors, and cultural expectations related to body image and performance.

Populations with elevated prevalence include university students, dancers, elite athletes, military recruits, and women following restrictive or unbalanced dietary practices. Estimates suggest that FHA may affect 10% to 30% of women in these higher-risk groups, although prevalence is likely underreported due to stigma surrounding stress, eating behaviors, and menstrual irregularities. Furthermore, FHA often manifests in women with normal reproductive anatomy and normal BMI, making it a diagnostic challenge and contributing to delayed recognition and intervention.

3.6 Summary

Functional hypothalamic amenorrhea arises from the synergistic interplay of psychological, metabolic, and physical stressors, with chronic activation of the HPA axis serving as a central pathophysiological mechanism. Identifying at-risk individuals requires careful assessment of lifestyle behaviors, dietary patterns, stress exposure, and menstrual history. Early recognition is essential to prevent long-term sequelae, including infertility, metabolic impairment, reduced bone mineral density, and neurocognitive consequences associated with chronic hypoestrogenism. A comprehensive understanding of FHA epidemiology and risk determinants provides a foundation for evidence-based prevention, informed clinical decision-making, and development of targeted therapeutic approaches.

4. Clinical Consequences

Functional hypothalamic amenorrhea (FHA) is a disorder with multifaceted clinical consequences, affecting not only reproductive health but also metabolic, skeletal, and neurological systems. The complex interplay of hormonal dysregulation, energy deficiency, and chronic stress underlies these wide-ranging effects.

4.1 Reproductive Dysfunction

The most immediate clinical consequence of FHA is anovulation and menstrual irregularities. Suppressed pulsatile secretion of gonadotropin-releasing hormone (GnRH) leads to reduced production of luteinizing hormone (LH), follicle-stimulating hormone (FSH), and estrogen, resulting in oligomenorrhea or complete amenorrhea (Berga et al., 1989; Gordon et al., 2020/2021). Prolonged suppression of the hypothalamic–pituitary–ovarian (HPO) axis may impair fertility and pose challenges for conception. In addition, altered sex hormone levels can disrupt endometrial development, potentially affecting implantation and early pregnancy maintenance.

4.2 Bone and Skeletal Health

Chronic estrogen deficiency in women with FHA contributes to reduced bone mineral density, increasing the risk of osteopenia and osteoporosis. Evidence suggests that bone mass deficits may develop early in life, with long-term implications for skeletal health and fracture risk in later adulthood (Laughlin & Yen, review article; Gordon et al., 2020/2021). Energy deficiency and intensive physical training exacerbate these skeletal changes, particularly in women with low BMI or those following restrictive diets (Smith-Rogers et al., 2025). Early intervention to restore hormonal balance is critical for the prevention of irreversible bone loss.

4.3 Metabolic and Endocrine Consequences

FHA is associated with chronic HPA axis activation, leading to hypercortisolemia. Elevated cortisol exerts multiple metabolic effects, including dysregulation of glucose and lipid metabolism, insulin resistance, and alterations in thyroid hormone activity (Berga et al., 1988; Schaefer et al., 2018). Over time, sustained hypercortisolemia may increase the risk of cardiovascular disease and contribute to metabolic syndrome. Additionally, hormonal disturbances may affect appetite regulation, energy expenditure, and body composition, further compounding reproductive and skeletal risks.

4.4 Neurological and Psychological Effects

Chronic stress and elevated cortisol levels can impair cognitive function, mood regulation, and neuroprotection. Studies indicate that menstrual disturbances may serve as a clinical marker of prolonged stress exposure, potentially predicting long-term neurological consequences such as hippocampal atrophy, heightened susceptibility to mood disorders, and anxiety (Bikle et al., 2016). Psychological comorbidities, including depression and heightened stress reactivity, are frequently observed in women with FHA, creating a feedback loop that can further suppress reproductive function.

4.5 Additional Clinical Implications

Women with FHA may also experience alterations in cardiovascular and gastrointestinal function, primarily due to chronic energy deficiency and excessive physical activity (Gordon et al., 2020/2021; Barbagallo et al., 2023). Persistent FHA can result in multifactorial health consequences that require a multidisciplinary therapeutic approach, including psychological support, nutritional interventions, and structured exercise modification. Early recognition and comprehensive management are essential to restore menstrual function, protect reproductive potential, and mitigate long-term systemic complications.

5. Diagnostic Evaluation

The diagnosis of functional hypothalamic amenorrhea (FHA) is complex and requires a systematic approach, including the exclusion of organic causes of menstrual disturbances and a thorough assessment of psychological, metabolic, and physical factors. Accurate and timely diagnosis is essential for preventing long-term reproductive and systemic complications.

5.1 Clinical History and Physical Examination

A comprehensive clinical history is the cornerstone of FHA diagnosis. Key elements include age at menarche, menstrual cycle regularity, body weight trajectory, dietary habits, level of physical activity, and exposure to psychosocial stressors (Gordon et al., 2020/2021). It is also critical to identify eating disorders, disordered eating behaviors, and signs of chronic psychological stress. Physical examination should include assessment of body mass index (BMI), body composition, signs of androgen excess, and clinical indicators of nutritional deficiencies. Subtle findings, such as delayed secondary sexual characteristics or decreased subcutaneous fat, may provide additional diagnostic clues.

5.2 Hormonal Assessment

Hormonal evaluation is essential to assess the function of both the hypothalamic–pituitary–adrenal (HPA) and hypothalamic–pituitary–ovarian (HPO) axes. Commonly measured parameters include:

- Gonadotropins (LH, FSH)
- Estrogens (estradiol)
- Progesterone
- Cortisol and adrenocorticotropic hormone (ACTH)

These measurements provide insight into both reproductive suppression and stress-axis hyperactivity (Berga et al., 1988; Richards et al., 2000; Schaefer et al., 2018). In selected cases, dynamic testing, such as corticotropin-releasing hormone (CRH) stimulation or GnRH testing, may be performed to evaluate hormonal reserve and neuroendocrine responsiveness, further clarifying the etiology of menstrual suppression (Richards et al., 2000; Barbagallo et al., 2023).

5.3 Imaging and Additional Studies

Imaging studies are indicated to exclude organic causes of amenorrhea, such as pituitary tumors or hypothalamic lesions. Magnetic resonance imaging (MRI) of the pituitary is the standard modality. In patients with prolonged FHA or a history of energy deficiency, assessment of bone mineral density using dual-energy X-ray absorptiometry (DXA) is recommended to quantify osteoporosis risk and guide long-term management (Laughlin & Yen, review article; Gordon et al., 2020/2021).

5.4 Differential Diagnosis

FHA remains a diagnosis of exclusion. Differential diagnosis should include:

- Primary or secondary amenorrhea due to ovarian, pituitary, or hypothalamic disorders
- Endocrine disorders such as hypothyroidism or hyperprolactinemia
- Eating disorders with severe energy deficits, which may require specialized interventions distinct from FHA management (Smith-Rogers et al., 2025; Barbagallo et al., 2023)

A careful evaluation of clinical context, hormonal profile, and imaging findings is crucial for accurate differentiation and avoiding misdiagnosis.

5.5 Clinical Indicators and Monitoring

Ongoing monitoring of menstrual patterns, body weight, dietary habits, and physical activity levels is essential for assessing the effectiveness of therapeutic interventions. Menstrual irregularities can serve as sensitive indicators of chronic stress and energy deficiency, enabling early identification of women at risk for long-term reproductive, skeletal, and metabolic consequences (Bikle et al., 2016; Laughlin & Yen, review article). Integration of clinical, hormonal, and lifestyle data provides a comprehensive framework for individualized care planning and preventive strategies.

6. Therapeutic Management

The management of functional hypothalamic amenorrhea (FHA) requires a comprehensive, individualized, and multidisciplinary approach. The primary objectives of therapy are to restore the normal function of the hypothalamic–pituitary–ovarian (HPO) axis, re-establish regular menstrual cycles, protect bone density, optimize metabolic and cardiovascular health, and improve overall psychological and physical well-being. Treatment strategies are designed to address the multifactorial etiology of FHA, including energy deficiency, excessive physical activity, and chronic psychological stress.

6.1 Lifestyle Optimization and Nutritional Interventions

A positive energy balance is the cornerstone of FHA therapy. Restoration of adequate caloric intake should match or exceed the patient's energy expenditure, with particular attention to the distribution of macronutrients. Protein intake supports muscle mass and bone health, while sufficient carbohydrate intake ensures normal hypothalamic signaling and prevents excessive cortisol secretion. Micronutrients, including calcium, vitamin D, magnesium, and vitamin K, are essential for bone metabolism and reproductive function (Smith-Rogers et al., 2025; Gordon et al., 2020/2021).

Lifestyle modifications should also address physical activity. While exercise has numerous health benefits, excessive training in combination with energy deficiency can exacerbate menstrual dysfunction. Gradual reduction of exercise intensity or frequency, combined with supervised training programs, allows for safe restoration of energy balance without abrupt loss of fitness or psychological stress. Tailoring activity to the patient's nutritional status and menstrual recovery is recommended.

6.2 Psychological Support and Stress Management

Chronic psychological stress is a major contributor to FHA, and psychological interventions are critical. Cognitive-behavioral therapy (CBT) has demonstrated efficacy in reducing maladaptive thought patterns, managing anxiety, and promoting behavioral changes that support dietary adherence and exercise moderation (Bikle et al., 2016; Barbagallo et al., 2023).

Other stress-reduction techniques, including mindfulness-based stress reduction (MBSR), relaxation exercises, guided imagery, and biofeedback, may normalize hypothalamic–pituitary–adrenal (HPA) axis function and reduce hypercortisolemia, supporting the restoration of pulsatile gonadotropin-releasing hormone (GnRH) secretion (Schaefer et al., 2018; Gordon et al., 2020/2021). Psychological support also facilitates adherence to long-term lifestyle interventions, which is crucial for sustained recovery.

6.3 Pharmacological Interventions

In patients with persistent amenorrhea despite optimal lifestyle and psychological interventions, hormonal therapy may be indicated. Estrogen therapy, often in combination with progestogens, is primarily aimed at preserving bone mineral density, preventing osteoporosis, and supporting reproductive function (Laughlin & Yen, review article; Barbagallo et al., 2023).

Other pharmacological strategies may include selective estrogen receptor modulators (SERMs) or low-dose pulsatile GnRH therapy in specialized centers to restore ovulation in patients seeking fertility. Pharmacological interventions should be used as adjuncts to, not replacements for, lifestyle and psychological management. Careful monitoring of hormone levels, bone density, and cardiovascular markers is essential to ensure efficacy and safety.

6.4 Monitoring and Long-term Management

Continuous monitoring of menstrual function, hormonal profiles (LH, FSH, estradiol, cortisol), bone density (DXA scans), nutritional status, and physical activity is necessary to evaluate therapeutic response. Early detection of relapse allows timely adjustment of interventions. Regular follow-up also provides opportunities to address psychological well-being, identify new stressors, and prevent long-term complications.

6.5 Multidisciplinary Approach

Effective management of FHA is most successful in a multidisciplinary framework, involving endocrinologists, gynecologists, dietitians, psychologists, and physiotherapists. Such collaboration ensures that energy balance, hormonal health, bone preservation, and psychological resilience are addressed simultaneously. Long-term strategies should focus on sustaining healthy lifestyle habits, preventing recurrence, and supporting fertility when desired.

6.6 Preventive Strategies

Beyond acute treatment, preventive measures are important for at-risk populations, including female athletes, adolescents, and women under chronic stress. Education on energy requirements, healthy exercise patterns, stress management, and early recognition of menstrual irregularities can reduce the incidence of FHA and its associated health risks.

7. Discussion

Functional hypothalamic amenorrhea (FHA) represents a complex reproductive disorder with multifactorial etiology, encompassing interactions between psychological, metabolic, and physical factors. Current literature consistently highlights that chronic psychological stress, energy deficiency, and excessive physical exercise are the primary determinants of hypothalamic–pituitary–gonadal (HPG) axis suppression and subsequent menstrual disturbances.

Neuroendocrinological analyses emphasize the central role of hypothalamic–pituitary–adrenal (HPA) axis activation and elevated cortisol levels in inhibiting pulsatile gonadotropin-releasing hormone (GnRH) secretion. This suppression leads to hypoestrogenism, anovulation, and a cascade of clinical consequences, including decreased bone mineral density, reduced fertility, and potential long-term metabolic dysfunction (Berga et al., 1988; Schaefer et al., 2018). Understanding these pathophysiological mechanisms is essential for the effective management of FHA and for the prevention of chronic health complications.

Epidemiological data indicate that FHA predominantly affects women aged 18–35 years, particularly university students, competitive athletes, and individuals adhering to restrictive dietary regimens (Gordon et al., 2020/2021; Smith-Rogers et al., 2025). Diagnosis is often challenging due to the absence of structural abnormalities and the presence of normal body mass index (BMI) in many patients (Richards et al., 2000). This underscores the importance of detailed medical history, lifestyle assessment, and continuous monitoring of menstrual patterns to identify FHA early.

Therapeutically, a multidisciplinary approach combining lifestyle optimization, psychological support, and, in selected cases, hormonal therapy has shown the greatest efficacy (Laughlin & Yen, review article; Barbagallo et al., 2023). Non-pharmacological interventions, including restoration of energy balance, moderation of excessive physical activity, and cognitive-behavioral therapy (CBT), have demonstrated effectiveness in reestablishing menstrual cycles and normalizing HPG axis function. Hormonal therapy should complement these interventions, primarily to protect bone health and support reproductive function (Barbagallo et al., 2023).

Despite substantial research, significant knowledge gaps remain regarding individual susceptibility to stress and energy deficiency, as well as factors influencing the timeline for menstrual recovery. Prospective studies are needed to evaluate the long-term neuroendocrine, cognitive, and neurological consequences of FHA, particularly in relation to chronic stress exposure (Bikle et al., 2016).

In conclusion, FHA is a multifactorial disorder requiring an integrated diagnostic and therapeutic strategy. Early recognition and intervention can prevent long-term health complications and improve quality of life for women of reproductive age. Future research should focus on elucidating mechanisms underlying individual vulnerability to stress and energy deficiency, enabling more personalized and effective treatment approaches.

8. Conclusions

The current body of literature unequivocally demonstrates that chronic psychological stress constitutes a major and well-established risk factor for menstrual disturbances in women of reproductive age, including functional hypothalamic amenorrhea (FHA) (Berga et al., 1989; Gordon et al., 2020/2021). Long-lasting activation of the hypothalamic–pituitary–adrenal (HPA) axis promotes sustained hypercortisolemia, which disrupts the physiological pulsatility of gonadotropin-releasing hormone (GnRH) and consequently suppresses the activity of the entire hypothalamic–pituitary–gonadal (HPG) axis. This neuroendocrine dysregulation leads to diminished secretion of gonadotropins, a reduction in circulating estrogen levels, and the development of clinical manifestations such as oligomenorrhea, anovulation, or complete amenorrhea (Berga et al., 1988; Richards et al., 2000; Schaefer et al., 2018). Increasing evidence also suggests that the stress-related neuroendocrine alterations may interact with metabolic signals—including leptin, insulin, and ghrelin—thereby amplifying reproductive suppression in states of energy deficiency.

Accurate diagnosis of FHA requires a thorough and multidimensional clinical assessment encompassing lifestyle behaviors, nutritional patterns, physical activity levels, and psychological stressors (Smith-Rogers et al., 2025; Gordon et al., 2020/2021). In addition to detailed patient interviews and physical examinations, targeted hormonal evaluations are indispensable for differentiating FHA from organic etiologies of menstrual dysfunction, including pituitary adenomas, thyroid disorders, or hyperprolactinemia (Barbagallo et al., 2023; Richards et al., 2000). Evaluation of metabolic status and markers of chronic energy deficiency further enhances diagnostic precision. Moreover, bone mineral density (BMD) assessment using dual-energy X-ray absorptiometry (DXA) is of particular importance in individuals with prolonged amenorrhea, given the well-documented detrimental effects of hypoestrogenism on bone turnover, peak bone mass, and long-term skeletal integrity (Laughlin & Yen, review article; Gordon et al., 2020/2021). Early detection of bone demineralization is critical, as BMD losses incurred during FHA can be only partially reversible.

Effective management of FHA necessitates a comprehensive, multidisciplinary, and individualized therapeutic approach that acknowledges the complex interplay of psychological, metabolic, and behavioral factors. Core components of treatment include:

Lifestyle optimization and nutritional interventions: Restoration of adequate energy availability remains a cornerstone of FHA therapy. Achieving a stable, healthy body weight, normalizing macronutrient distribution, and reducing excessive levels of physical activity are essential for reestablishing HPG axis function (Smith-Rogers et al., 2025; Gordon et al., 2020/2021). Dietary counseling supports improved caloric intake, micronutrient sufficiency, and sustainable eating patterns. Interventions targeting energy balance have been shown to enhance endocrine recovery even in women with longstanding amenorrhea.

Psychological support: Structured psychological interventions—particularly cognitive-behavioral therapy (CBT)—play a pivotal role in modulating stress responses, improving coping strategies, and reducing maladaptive behaviors that perpetuate neuroendocrine dysfunction (Bikle et al., 2016; Barbagallo et al., 2023). Stress-reduction techniques, relaxation training, and strategies aimed at improving emotional regulation have demonstrated efficacy in reinstating reproductive function. Importantly, psychological support enhances adherence to lifestyle and nutritional recommendations and may serve as a key determinant of long-term therapeutic success.

Hormonal therapy: In cases of persistent amenorrhea where lifestyle modifications and psychological interventions do not yield sufficient improvement, hormonal therapy may be considered as an adjunctive measure. Estrogen supplementation, typically administered in combination with progestins, aims primarily to protect bone health and mitigate the systemic effects of chronic hypoestrogenism, rather than to replace behavioral and nutritional interventions (Laughlin & Yen, review article; Barbagallo et al., 2023). Continuous monitoring of bone density, endocrine markers, and treatment tolerance is essential to ensure optimal outcomes and prevent adverse effects.

Early identification of predisposing factors and timely implementation of a comprehensive therapeutic strategy not only facilitate the restoration of regular menstrual cycles but also substantially reduce the likelihood of long-term sequelae, including osteoporosis, metabolic dysregulation, chronic HPA axis hyperactivation, and impaired fertility (Laughlin & Yen, review article; Berga et al., 1989). Recognition of FHA as a multifactorial condition underscores the need for coordinated care across medical, nutritional, and psychological domains.

In summary, functional hypothalamic amenorrhea exemplifies a complex disorder in which psychological, metabolic, and environmental influences converge to disrupt reproductive physiology. An integrated diagnostic and therapeutic framework—encompassing detailed lifestyle assessment, psychological and nutritional support, and, when warranted, hormonal therapy—is essential for effective management. Such a holistic approach not only promotes recovery of menstrual function but also minimizes long-term health consequences, thereby supporting the overall well-being of women in their reproductive years.

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