Proceedings of ICBioMed 2025 Symposium: AI for Healthcare: Advanced Medical Data Analytics and Smart Rehabilitation
DOI: 10.54254/2753-8818/2025.AU25853

Hormonal Fluctuations and Mood Disorders Across the Menstrual Cycle

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Abstract. The menstrual cycle is an important feature of female reproductive physiology, and its association with psychological factors is increasingly understood. Studies have found that fluctuations in estrogen and progesterone during the menstrual cycle can affect mood, cognition, and emotion regulation. Subsequent studies have had some success in attributing hormonal changes to neurotransmitter systems and brain regions that regulate emotional function. However, these findings still leave some unanswered questions, especially why some women experience severe symptoms such as premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD). This article explores the various hormonal phases of the menstrual cycle and their effects on mood through neurobiological mechanisms, including the effects of estrogen on serotonin and dopamine, and the effects of progesterone on GABA-A receptors. It then explores the role of brain structures such as the amygdala and prefrontal cortex, as well as treatment strategies such as selective serotonin reuptake inhibitors (SSRIs), cognitive behavioral therapy (CBT), and lifestyle interventions. This article explores the effects of hormones on mood through an integrated perspective, which helps to deepen the understanding of mental health during menstruation and demonstrates the need for supportive public health policies. Future research could explore genetic susceptibility, long-term effects of birth control, and culturally sensitive approaches to better address and normalize hormone-related mood disorders.

Keywords: Menstrual Cycle, Hormones and Mood, Neurobiology of Emotion, Premenstrual Syndrome (PMS).

1. Introduction

The Mexican-American War (1846–1848) ended with the Treaty of Guadalupe Hidalgo, in which Mexico transferred over 500,000 square miles of land to the United States, including California, Arizona, New Mexico, and parts of several other states (p. 379–380). This gigantic territorial acquisition is called the Mexican Cession.

But this victory also energized sectional tensions in the U.S. over the extension of slavery. When states were being added, there were furious debates over whether slavery would be legal in them or not. This was especially seen in the Wilmot Proviso, a bill to prohibit slavery in the newly acquired territories (p. 380), that further divided the North and South.

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As cited by the CrashCourse video, host John Green highlights how the expansion revived the slavery controversy, ultimately leading to more Congress polarization, the rise of the sectional political parties, and finally the secession crisis. Hence, although the war fulfilled Manifest Destiny, it set the stage for the Civil War directly by bringing the war over slavery into national consciousness.

Menstrual cycle is a tightly regulated, hormonally controlled biological phenomenon that is the peak of the reproductive well-being of women. Besides the physical appearance, the menstrual cycle is increasingly being associated with long-term ramifications over emotional and mental states. Mood swings, irritability, anxiety, and depression are commonly observed in women, primarily the premenstrual phase. They may interfere with school and occupational functioning, work productivity, and interpersonal relationships, as well as physical well-being. While prevalent, the biological etiology of such mood change is downplayed in popular and clinical lore [1].

Recent medical and psychological science has documented an indubitable link between hormonal fluctuation and mood control. In particular, fluctuation in estrogen and progesterone levels during the menstrual cycle has been found to impact central neurotransmitters like serotonin, gamma-aminobutyric acid (GABA), and dopamine [2-4]. For example, elevated estrogen during the follicular phase is linked to heightened serotonin activity and good mood. The late luteal phase, on the other hand, is characterized by a sharp decrease in both estrogen and progesterone whose interference with neurotransmitter homeostasis could be accountable for premenstrual symptoms [5]. The impact of such hormonal fluctuations is most severe in women with heightened neurobiological sensitivity, creating conditions such as Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD) [6,7].

Evidence from a progressively larger group of biochemical as well as neuroimaging studies provides evidence for the function played by hormonal modulation of brain regions concerned with emotional processing, including the amygdala, prefrontal cortex, and hypothalamus [8,9]. For instance, functional MRI research has revealed increased sensitivity of the amygdala in females with PMDD in the luteal phase, which would be consistent with a biological origin of their affective symptoms. In addition, the progesterone metabolite allopregnanolone has been found to modulate GABA-A receptors, and withdrawal from it can cause the concomitant anxiety and mood lability of premestrum [3,10]

Education for clinical practice as well as for activism regarding the neurobiological mechanisms of hormone-related mood changes is required. Although effective treatments such as psychological counseling (Cognitive Behavioral Therapy, CBT) and medications, such as Selective Serotonin Reuptake Inhibitors (SSRIs) and hormonal contraceptives are available, many women remain undiagnosed and untreated because of stigma, misdiagnosis, or lack of awareness. Public health strategies should bridge this gap by establishing menstrual mental health sensitivity and support cultures in schools and workplaces [11].

The paper attempts here to provide a critical review of current medical literature on the relationship between endocrine alterations with menstrual cycles and impact on mood. The paper begins with summaries of hormone patterns during different phases of the cycle, followed by neurobiological effects on brain function and neurotransmitters. This paper goes on to describe evidence-based intervention strategies before ending with recommendations for how support for women's emotional well-being can be improved at a societal level. By being focused on the scientific basis of mood fluctuation with hormones, this research encourages a softer and more evidence-based approach to women's health.

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2. Menstrual cycle hormonal patterns

2.1. Menstrual cycle phases

The mean 28-day menstrual cycle is traditionally divided into four stages: the follicular stage, ovulation, the luteal stage, and menses. Each is characterized by distinct endocrine changes and accompanying physiological and behavioral events. The follicular phase begins with menstruation and is dominated by rising estrogen levels, which lead to thickening of the uterine lining and maturation of ovarian follicles. Ovulation occurs mid-cycle due to a surge of luteinizing hormone (LH), leading to the excretion of a mature egg. Once ovulation has occurred, luteal phase starts and is marked by the dominance of progesterone, secreted by corpus luteum, and balanced estrogenic levels. Upon failure of fertilization, hormone levels plummet precipitously, initiating menstruation and the onset of a fresh cycle [1,2].

2.2. Estrogen balance and mood impact

Estrogen is mainly accountable for regulating mood and emotions during the menstrual cycle via its mechanism on neurotransmitter systems such as serotonin and dopamine. Since estrogen levels rise slowly during the follicular phase, it stimulates the secretion and accessibility of serotonin, which correlates with improved mood, emotional stability, and energy [3]. This phase is usually marked by improved cognitive performance and pleasant affective states, as supported by neuroimaging research conducted by Martinez et al., where functional MRI was employed to monitor brain activity in 27 healthy women at different phases of their menstrual cycles. The study found that at the mid-follicular stage, as estrogen was increasing, the subjects had significantly increased activity in the ventral striatum and orbitofrontal cortex, regions associated with reward sensitivity and emotional regulation. Statistical examination indicated a positive association between serum estrogen levels and BOLD response in these regions and correlation coefficients of $r = 0.42$ to $r = 0.61$, which illustrated a moderate to strong relationship between reward-processing neural activation and levels of estrogen [4].

The ovulatory surge of estrogen can also heighten social intimacy and positive mood. These are transient, however, as estrogen levels plummet after ovulation and during the luteal phase. This decline in estrogen, and particularly when preceded by increased progesterone, has been associated with irritability, anxiety, and depressive symptoms in females [5]. The intensity of these mood disturbances is believed to be mediated by the range of fluctuation in estrogen sensitivity and starting neurochemical status [6].

2.3. Cycles of progesterone change and mood impact

In contrast to estrogen, the action of progesterone on mood is more multifaceted and usually dampening. Following ovulation, progesterone concentrations begin to risefollowing ovulation and reach 10–20 ng/mL at the mid-luteal peak in ovulating women, as seen in serum hormone assays. These high levels play a central role in mood regulation by acting through the GABA-A receptors via the neurosteroid allopregnanolone. Progesterone, through its metabolite allopregnanolone, influences GABA-A receptors in the brain, which mediate inhibitory neurotransmission and control over anxiety [7]. Allopregnanolone is anxiolytic and sedating in moderate doses. Paradoxical effects of dysphoria, sedation, and impaired cognition can arise when concentrations shift too quickly or otherwise increase [8].

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Furthermore, abrupt progesterone and metabolite withdrawal during the impending menses has also been linked with pronounced mood lability in vulnerable women. Progesterone concentrations begin to rise following ovulation and peak at mid-luteal phase with levels of approximately 10–20 ng/mL in ovulating women, as observed in serum hormone research. The elevated levels play a role in mood control via action on the GABA-A receptors in the form of the neurosteroid allopregnanolone. Such women with heightened vulnerability to neurosteroid change are particularly susceptible to PMDD, where progesterone dynamics have been argued to be an underlying pathophysiological mechanism [10].

2.4. The time of combined hormone interaction and vulnerability

Although both estrogen and progesterone have individual roles to play in emotional control, more often than not the interaction and rate of change between them, particularly the precipitous changes toward the late luteal phase, is responsible for mood disturbances. It is not the absolute levels of the hormones that are responsible for many of the emotional symptoms but the instability and imbalance between estrogen and progesterone [11].

This is made possible by research that confirms that women with PMDD exhibit normal hormone levels but react in a different way to their fluctuation. Experimental hormone suppression and reintroduction models have confirmed that symptom activation is strongly correlated with fluctuations in hormonal milieu rather than baseline levels. This window of concurrent hormonal variation, particularly in the five to seven days prior to menstruation, is where most reported cases of premenstrual dysregulation of mood take place, which suggests a window of vulnerability in women with pre-existing neuroendocrine sensitivity [6,9].

2.5. Neuroendocrine sensitivity and mood disorders (PMS & PMDD)

PMS and its more disabling variant, PMDD, are clinical manifestations of menstrual cycle–related mood disorders. PMS is characterized by a pattern of emotional and somatic symptoms—irritability, tension, fatigue, and sadness—that are confined to the luteal phase and remit soon after menses begin. PMDD, on the other hand, is characterized by more incapacitating and marked symptoms—extreme mood swings, hopelessness, irritability, and interpersonal conflict—that substantially impair daily functioning [7,10].

Pathophysiology of PMDD is rooted in heightened neural sensitivity to normal variations in ovarian steroids. Women with PMDD exhibit abnormal brain responses in the emotional regulation networks of the brain, particularly in the amygdala and prefrontal cortex, during the luteal phase. Functional MRI research has established hyperactivation of the amygdala during emotional stimulation, in accordance with mood reported instability [8,9]. Further, impairment of the serotonergic and GABAergic systems has been linked to the pathogenesis of PMDD, providing a biochemical rationale for its pharmacotherapy with SSRIs and hormonal control treatments [5,7,11].

3. Neurobiological effects of endocrine fluctuations

3.1. Typical symptoms and theoretical models

Mood symptoms of the menstrual cycle—irritability and anxiety, through to severe sadness and cognitive impairment—have been explained by a number of theoretical models. The most popular of them is the neuroendocrine sensitivity hypothesis, which assumes that a subgroup of women possess a biological susceptibility to overreact to normal hormonal variation [6]. It follows from this model

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that it is understandable that all women are not afflicted with PMS or PMDD, though they experience the same hormone cycles.

One such alternative model is the allopregnanolone sensitivity hypothesis, which highlights progesterone's neurosteroid metabolite's seemingly paradoxical actions on GABA-A receptors. This model is supported by evidence that acute shifts in allopregnanolone levels possess the potential to cause symptoms such as emotional dysregulation, panic, and impaired stress resilience [3,8].

3.2. Involvement of neurotransmitters

Several important neurotransmitters are involved in the mediation of hormonal change on mood. Serotonin, which is directly linked to wellbeing and emotional balance, has been found to be affected by estrogen. Estrogen increases receptor density and serotonin synthesis, causing enhancement of mood during the follicular phase [4]. Low levels of estrogen, as in the luteal phase, can potentially decrease serotonergic activity, causing irritability and low mood [5].

GABA is also an important neurotransmitter that is affected by hormonal change, namely by the action of allopregnanolone on GABA-A receptors. These receptors are involved in the suppression of neuronal excitability, and their deregulation is associated with anxiety and panic disorders. Fluctuations in allopregnanolone—most importantly its withdrawal just before menstruation—may lead to reduced GABAergic inhibition with consequent mood destabilization [3,7].

Dopamine, involved in reward and motivation, is also modulated by estrogen. Literature shows that estrogen can enhance dopaminergic transmission in certain brain regions, producing pleasure, focus, and sociability during ovulation. When estrogen levels drop in the luteal phase, dopaminergic tone may also drop, possibly explaining anhedonia and lack of motivation [2,10].

3.3. The function of brain areas in mood modulation

A number of brain areas are involved in the modulation of emotions and are sensitive to ovarian hormone fluctuations. Of the most important of these areas whose function is pertinent to mood regulation and cognitive-affect integration, the amygdala, prefrontal cortex (PFC), and hypothalamus stand out.

The amygdala is engaged predominantly in affectively valent stimulus processing, specifically fear or danger stimuli. Progesterone and estrogen modulate amygdala responsivity: fMRI has shown enhanced responsivity of the amygdala during the luteal phase of the menstrual cycle, especially in women with PMDD, related to heightened anxiety and emotional sensitivity [4,8].

Prefrontal cortex, particularly ventromedial and dorsolateral areas, is responsible for top-down regulation of emotional response. Working of PFC is reduced during low estrogen phases (luteal phase) that may interfere with cognitive control of negative emotion [9]. Cycles of high estrogen have been said to be characterized by high PFC and executive function efficiency, resulting in emotion stability in the follicular phase [4].

Hypothalamus, a site of control by the endocrine system, also decodes messages for reproductive and stress hormones. It controls the action of the hypothalamic-pituitary-adrenal axis, which is countered by fluctuations of a cyclic nature in hormones. Hormonal fluctuation in late luteal phase was seen to interfere with HPA axis function with resultant mood liability [10].

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3.4. Biochemical and imaging evidence of mood-hormone relationship

Neuroimaging and biochemistry research, nonetheless, preferentially favor the connection among hormonal change and brain activity that is related to mood.

In a pioneering study by Baller et al., PMDD women exhibited heightened amygdala activity to emotional stimuli during the luteal phase, whereas healthy controls exhibited relatively homogeneous patterns [4]. Gingnell et al. also found that estrogen therapy decreased amygdala activity and noted other stabilizing, protective influences of estradiol on affective reactivity [8].

Biochemically, GABA and serotonin are controlled by hormonal fluctuation. Estrogen activates the tryptophan hydroxylase rate-limiting enzyme for serotonin production, while progesterone (via allopregnanolone) modulates the sensitivity of the GABA-A receptor. Neuroendocrine challenge tests under suppression with GnRH agonist and hormone add-back trials confirmed that symptomology of mood in PMDD is due to hormone fluctuation, not absolute hormone levels [2,6].

4. Intervention strategies and public health recommendations

4.1. Psychological interventions

CBT, or psychological therapies, is a first-line therapy for PMS and PMDD. CBT focuses on reversing negative thoughts, affect regulation, and behavioral activation. CBT reduces the severity of PMDD by 40–50% in controlled trials [1]. Two additional therapies are mindfulness-based stress reduction (MBSR) and dialectical behavior therapy (DBT), which enhance awareness of feelings and reduce rumination.

4.2. Pharmacolog`ical treatments

SSRIs are the medication of first choice for the drug therapy of PMDD. SSRIs enhance the serotonergic neurotransmission lost in the withdrawal phase. SSRIs block the reuptake of the serotonin into the presynaptic neuron and thus enhance the concentration of serotonin in the synaptic cleft. Medications like fluoxetine and sertraline have been successful with steady and luteal-phase dosing regimens, more than 60% better in trials [5,11]. Drospirenone hormone pills contraceptives, low estrogen especially, balance out hormonal imbalance.

5. Conclusion

The endocrine cycling of the menstrual cycle—i.e., estrogen and progesterone—influences greatly brain function and mood regulation. The hormones in turn influence intellectual dominance and emotional stability through the control of neurotransmitters such as serotonin, GABA, and dopamine. Vulnerable patients develop PMS or PMDD from increased neuroendocrine hypersensitivity, supported by neuroimaging and biochemical data.

Therapeutic strategies, including CBT, SSRIs, hormonal contraception, and supportive lifestyle change, yield adequate remission of symptoms. More extensive public health strategies—public raising of awareness, increased diagnosis, and offering school/workplace support—are needed to improve women's health. Additional research into the neurobiology of the menstrual cycle will continue to offer a connection between clinical practice and women's experience.

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