“The Menstrual Cycle's Impact on the Brain and Mood: Understanding PMDD”

Abstract

The Premenstrual Dysphoric Disorder (PMDD) is a type of disorder that approximately only 5 percent of women experience during the luteal phase of their menstrual cycle, and is clinically diagnosed as a depressive disorder. Due to the little amount of people experiencing and carrying the knowledge about PMDD, and how changes during the menstrual cycle, especially luteal phase, can result in emotional changes, and even depression. In this study, past researches about PMDD were reviewed and analyzed to find out the causes of PMDD. It was discovered that

women with PMDD different brain structures which resulted in abnormal reactions to hormonal fluctuations, ultimately causing emotional dysregulation. Additionally, researchers have found that they have different brain activities in certain brain regions that control emotions. This may result in emotional symptoms and even affect decision making. Brain network changes were also observed and it was concluded that in PMDD, the brain interaction is all over the place, which makes it harder to control emotions. Although this disorder causes severe psychological effects, there are still no standardized treatments.

Introduction

The menstrual cycle is regulated by fluctuations in hormones like estrogen and progesterone, which rise and fall throughout the month. Research suggests that these changes not only affect the body but also influence mood and thinking, particularly during the luteal

phase. In addition, research also indicates that ovarian hormonal changes can cause psychological disorders. Many women experience mood swings and anxiety before their period due to a drop in estrogen, showing that hormone changes can affect emotional regulation (Albert et al. 2015). The finding of brain scans used during the menstrual cycle that proves emotional sensitivity in the days before menstruation, only furthers this argument (Gingell et al. 2012). These evidences may be due to the peaking of the progesterone levels during the luteal phase where it increases the risk of addictive vulnerability and causes memory enhancement of negative experiences (Andreano et al. 2019). The psychological changes during the menstrual cycle often occur during the luteal phase, a finding relevant in premenstrual disorders such as Premenstrual Syndrome (PMS) and Premenstrual Dysphoric Disorder (PMDD), where PMDD is classified as a depressive disorder (Le et al, Ko et al. 2024). This supports the above claims as it directly demonstrates the molecular changes of emotional vulnerability during this phase. This research validates the idea that menstrual hormones can increase the possibility of having a psychological disorder, especially in adolescent women. On the positive side, women did better on cognitive tasks when estrogen levels were high. These studies all suggest that hormonal changes can affect both emotions and thinking. Most research focuses on the initial emotional and cognitive effects of the menstrual cycle on adult women, but those who explore the negative psychological and mental effects it has. This study will explore the changes in estrogen and progesterone levels during luteal phase affect the severity of depression or anxious symptoms in individuals with Premenstrual Dysphoric Disorder (PMDD), from a neurophysiological perspective.

Literature Review

PMDD definition and classification

Premenstrual Dysphoric Disorder (PMDD) is a cyclic hormone-based mood disorder ("What is PMDD"). PMDD is considered the most severe psychological form of Premenstrual Syndrome (PMS) and is classified as a depressive disorder in the DSM-5 (Naik et al. 2023). It affects emotional and physical health during the luteal phase. Individuals with PMDD often experience affective liability, irritability, depressed mood, and anxiety in addition to physical symptoms like fatigue or bloating (Dorwart, 2023). These symptoms often occur during the luteal phase and interfere with the individual's daily life, especially among adolescent women (Naik et al. 2023).

Symptoms and Diagnosis

Diagnosing PMDD can be challenging since healthcare providers primarily rely on the patients self reported symptoms. According to the DSM-5, to be diagnosed with PMDD you must experience at least five physiological or physical symptoms in the week before your period, and it must only be present during your menstrual cycle (Dorwat, 2023).The key indicator they look for is the timing of the symptoms; they must occur at least 2 weeks before the start of the cycle (luteal phase) and subside shortly after the period starts. In order to help with diagnosis, self-screening tests such as IAPMD's "PMDs Self Screen" can help you recognize whether your symptoms align with PMDD, or Symptoms tracking tools like Daily Record of Severity Problems, which is used to confirm PMSS by rating more than two cycles daily symptoms. Because these tests or tools are mainly for assessments, clinical evaluation by a healthcare provider is necessary to confirm the diagnosis.

Scope and Prevalence

The scope of the individuals who experience PMDD has been analyzed by multiple researchers. PMDD affects up to 1 in 20 individuals who menstruate (Madormo 2025).

Compared to PMS, which approximately affects 80%, it is considerably low. In addition,most of those who have been diagnosed with PMDD have been prior diagnosed with anxiety or depression. Another research showed that 5% to 8% of women are affected (Mishra et al. 2023). It has also been suggested that “black women (2.9%) were significantly less likely than white women (4.4%) to experience PMDD (Pilver et al. 2010). Which raises the question on whether an individual's race is a risk factor for PMDD. These studies illustrate the importance of further research about this disorder as it has a large scope of estimated the possible number of women affected by PMDD. However due to the lack of research, there is still no concrete answer of concrete and more accurate data of individuals with PMDD, which opens opportunities for further research.

Hormonal Phases and Physiological Mechanisms

An average length of the Menstruation Cycle is typically 28 days. This cycle is divided into 4 phases; The menstrual phase, follicular phase, ovulation, and luteal.

The cycle begins with the menstrual phase and uterine lining shed, also known as a period. This occurs when pregnancy has not taken place, causing the levels of the hormones estrogen and progesterone to drop.

The follicular phase overlaps with the menstrual phase since it starts from the first day of the period and continues until ovulation. During this time hypothalamus signals the pituitary gland to release follicle-stimulating hormone (FSH), which stimulate the ovaries to produce follicles each containing an immature egg.

Third is the ovulation phase, which occurs when the rising estrogen levels caused by the previous phase trigger the pituitary gland to release luteinizing hormone (LH). This is also when the ovary releases a mature egg toward the uterus in preparation for fertilization.

Finally, the luteal phase is when the most changes in hormones take place. The egg that was

released by the follicle transforms to corpus luteum, which releases ovarian hormones progesterone and estrogen (Whelan 2019). During the luteal phase, progesterone levels rise and suddenly drop when pregnancy does not occur. This hormonal shift is believed to trigger emotional symptoms for PMS, and is the phase most closely linked to the risk of PMDD. PMDD symptoms usually appear during the luteal phase and disappear after a few days during menstruation due to the brain's sensitivity to the rise and fall of progesterone and estrogen ("What is pmdd?")

Hormonal Fluctuations and Brain interactions

Progesterone levels fluctuate throughout each phase of the menstrual cycle, and these changes are mirrored by its metabolite, allopregnanolone (ALLO), a positive allosteric modulator of the gamma-aminobutyric acid A ($GABA_A$) receptor (Gao et al 2023; Hantsoo and Epperson 2020). Several studies have also concluded that in PMDD, although the individual holds normal hormone levels, their brain reacts abnormally to typical ALLO fluctuations, causing emotional dysregulation (Gao et al 2023; Hantsoo and Epperson 2020).

GABA-A receptors are involved in regulating mood and anxiety. One of their many roles is to respond to gamma-aminobutyric acid GABA, a neurotransmitter that calms brain activity. When GABA binds to these receptors, it reduces neuronal firing and promotes relaxation and emotional stability. When GABA gets in contact with ALLO, its effect gets enhanced, making the brain more resistant to stress. The amount of ALLO changes with progesterone. Gao et al. (2023) Found out that a low dose of ALLO increases the possibility of PMDD-like symptoms. The same researcher confirmed that the ovarian hormones fluctuation can affect the pathogens of PMDD.

Organ (2023) summarized that during the luteal phase, increased ALLO usually enhances GABA-A receptor activity, which contributes to mood stabilization. However, in individuals

with PMDD, this process may not function as expected. Changes in GABA-A receptor sensitivity or function may alter how the brain responds to ALLO, reducing its calming effects. Rapid hormonal fluctuations may further impact GABAergic activity, potentially contributing to emotional symptoms and mood disturbances.

Brain Structure Differences

Beyond functional changes, structural MRI studies reveal that people with PMDD have anatomical differences in emotional brain regions. Specifically, Gray Matter Volume (GMV) is altered in areas like hippocampus and parahippocampal cortex which are key for memory and emotional regulation. Jeong et al. (2012) found increased gray matter density in the hippocampal cortex and decreased density in the parahippocampal cortex among PMDD individuals. Berman et al. (2013) reported greater GMV in the posterior cerebellum, which may reflect prolonged brain responses to emotional symptoms over time. These studies support the idea that individuals who have PMDD may have different brain structure, which may be one of the main factors why they have abnormal reactions to hormonal fluctuations.

Brain imaging of individuals with PMDD

Researchers found that people with PMDD have higher activity in a part of the brain called amygdala, which controls emotional responses. This means their brains may react more strongly to stress or negative emotions, especially during the luteal phase. Baller et al. (2013) discovered that women with PMDD showed more amygdala and prefrontal cortex activity during emotional tasks in the luteal phase compared to women without PMDD, the prefrontal cortex helps manage emotions and decision-making, and when it doesn't work properly, people may have trouble staying calm. Gingell et al. (2012) also found that even in women without PMDD, this emotional part of the brain becomes more active before their

period, which suggests that hormone changes play a big role. This proves that people with PMDD are extra sensitive to these normal hormonal changes.

Cognitive and Behavior Effects

Hantsoo and Epperson (2016) also explained that the physiological changes in neurotransmission and brain activity directly impact cognition and behavior. During the luteal phase, reduced serotonin and GABA signaling impair concentration, memory, and decision making, while brain regions involved in emotional regulation struggle to maintain calm. As a result, individuals may experience brain fog, impulsivity, irritability, and increased emotional reactivity (Wieczorec et al. 2023). These symptoms are rooted in neurobiological changes and not just simple physiological stress.

Stress sensitivity and HPA Axis Dysregulation

Hamidovi et al. (2024) found that in PMDD, the hypothalamic-pituitary-adrenal (HPA) axis manages stress responses via cortisol release, and is often hypo-reactive to acute stress, especially in the luteal phase. Women with PMDD show blunted cortisol rise during stress tests and a weakened awakening response and daily cortisol slope. This inadequate stress adaptation may stem from repeated hormonal stress cycles combined with baseline stress, leading to allostatic overload, which is a breakdown in the body's ability to manage stress effectively. Another research by Hantsoo et al. (2023) explained the interactions between HPA and HPG axes, particularly the influence of ALLO on cortisol regulation, further complicating stress response in those experiencing PMDD.

Brain Network Changes

Women with PMDD show decreased segregation, meaning brain regions interact more diffusely, and increased integration, which may make it harder to control emotions (Dan et al. 2020). They have weaker connections in the anterior temporal lobe and stronger connections in the thalamus and basal ganglia, areas linked to emotions. Additionally, a study of Petersen et al. (2019), reported that the executive control network (ECN), which helps manage emotions, also connects more strongly to other brain areas in PMDD, suggesting emotional processing hangers.

Treatments Mechanisms Based on Physiology

SSRIs are the primary treatment for PMSS and are distinctive in their rapid onset; many individuals see improvements within 1-3 days of the luteal phase, even at low doses. This quick response suggests that SSRIs do more than boost serotonin levels, they also enhance ALLO biosynthesis, acting as selective brain steroidogenic stimulants (SBSS). By increasing the conversions of progesterone metabolites via enzymes, SSRIs help normalize GABA-A receptor modulation and ease symptoms (Hantsoo and Epperson, 2020; Modzelewski et al, 2024). New GABA-modulating treatments, including synthetic ALLO, are under investigation and show promise in related disorders such as postpartum depression. This highlights the important do;e do neurosteroid pathways in PMD physiology (Hantsoo and Epperson, 2020).

Importance of the Study

Most women who have Premenstrual Dysphoric Disorder (PMDD) remain undiagnosed, largely due to the lack of research, awareness, and clinical training. This often leads to misdiagnosis, commonly anxiety or mood disorders. Without proper recognition, individuals may struggle to understand the emotional and physiological changes they may face, leading

to feelings of confusion, isolation, or distress. Research has shown that PMDD significantly increasaes the risk of suicidal thoughts and behavior (Yan et al. 2021). People around women who experience PMDD should understand the mental and physical toll it has on women and support them physically and emotionally. In addition, since there is still a lack of awareness about PMDD, there should be a demand for media coverage or explanations about PMDD's effects on women. This wouldn't just help the masses know about the disorder, but also inform women who possibly have it realize their symptoms. The importance of this study extends beyond medical understanding: it is about validating women's experiences and ensuring they feel seen, supported, and heard.

Methodology

1. Research Design

This study is a non experimental study, based on analyzing existing scientific literature on hormonal changes, brain structure, and brain alterations in PMDD.

2. Aim and Objectives

Aim: to explore how ovarian hormone fluctuations, particularly estrogen and progesterone, during the luteal phase impact emotional symptoms in individuals with PMDD from a neurophysiological perspective.

Objectives:

- Analyze hormonal effects on brain function related to mood regulation.
- review neuroimaging studies on brain structures and network changes in PMDD.
- To explore gaps in current literature for future research.

3. Source of Data

data will be collected from peer-reviewed journal articles, academy databases (PubMed, GoogleScholar, Jstore), and reputable health organizations' publications focusing on PMDD, brain imaging, and neurophysiology.

4. Theoretical Framework

This study emphasizes neurophysiology, focusing on how ovarian hormone fluctuations modulate brain activity, which influences mood and behavior.

5. Data Analysis Approach

A content analysis will be conducted to identify commentators and findings related to hormonal influence on brain structure, brain network, and symptom severity in PMDD.

6. Inclusion and Exclusion Criteria

Inclusion: studies published from 2000 onwards, focused on PMDD, hormonal effects on the brain, cognitive and behavioral changes caused by PMDD, treatments, menstrual cycle, and neuroimaging findings

exclusion: Studies focusing solely on PMS without PMDD differentiation, lack neurophysiological data, unpublished blogs or non-scientific sources.

7. Ethical Considerations

Since this study uses secondary data from published research, there is no direct human participation. Proper citations and respect for academic honesty and avoidance of plagiarism will be maintained.

8.Expected Outcomes

This study expects to clarify how hormone fluctuations during the luteal phase affect brain function and mood in PMDD, it aims to identify key brain regions and networks involved and help validate the experiences of those affected and encourage earlier diagnosis.

Conclusion

Premenstrual Dysphoric Disorder (PMDD) is the most severe variant of PMS and is clinically classified as a depressive disorder. It typically occurs during the luteal phase of the menstrual cycle and is characterized by symptoms such as irritability, mood changes, and anxiety. Although these symptoms are also present during the luteal phase and quickly disappear after a few days of period, they can significantly disrupt an individual's daily life as it has severe negative effects on their mental and physical health.

Current research suggests that PMDD is associated with an abnormal neurological response to hormonal fluctuations, which leads to cognitive and behavioural impairments. Specifically, the intersection between the GABA-A receptor and allopregnanolone (ALLO), which usually gives positive effects to the brain, appears to be different in individuals with PMDD, resulting in emotional dysregulation. Neuroimaging studies have provided further support for this, showing heightened activity in the amygdala and prefrontal cortex, brain regions involved in emotion regulation and decision-making. Additionally, structural differences such as altered Gray Matter Volume (GMV) in key areas for memory and emotion have been observed, reinforcing the notion that PMDD is not only psychological but also physiological in nature.

Despite these findings, there is currently still no standardized treatment. Additionally, public and clinical awareness of the disorder still remains limited. This lack of recognition often leads to misdiagnosis or confusion about emotional experiences, further complicating

the lives of those affected. Given the severity of its psychological and physiological effects, PMDD calls for greater scientific attention and increased efforts to toast the development of effective treatment strategies. This calls for more in depth research and demands to inform the masses about this disorder.

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