

Psychiatric symptoms on the ovarian hormone roller-coaster

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Summary

This themed issue examines the impact of ovarian hormone fluctuations on women's mental health across the lifespan, including puberty, the menstrual cycle, pregnancy, postpartum and menopause. It highlights critical gaps and calls for sex-specific approaches in reproductive psychiatry and hormone-informed mental care.

Keywords

Brain; hormones; menstrual cycle; mental health; women.

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Ovarian hormone fluctuations, such as those occurring during the menstrual cycle, pregnancy, postpartum and menopausal transition, mark critical windows of vulnerability for mental health. Moreover, despite the widespread use of hormonal contraceptives and hormone replacement therapies, their neuropsychiatric effects remain poorly understood. As researchers and clinicians, we frequently encounter surprise – even disbelief – from patients, the public and policymakers about the limited scientific understanding in this domain, especially given its relevance during some of the most meaningful phases in a woman's life.

At the intersection of the endocrine and nervous systems, ovarian hormones play a crucial role in mental health – impacting neurotransmission, neurogenesis, neuroinflammation, neuroprotection and synaptic plasticity. Their effects extend well beyond the hypothalamic–pituitary–gonadal axis, with receptors widely expressed in brain regions governing mood, cognition and reward processing. Gonadal steroids and their neurosteroid metabolites, such as allopregnanolone, cross the blood–brain barrier and directly affect the brain. In addition, neurons and glia are a source of local steroidogenesis. Acknowledging this functional interplay and transcending sex differences in psychiatry, attention in this themed issue is drawn to women's mental health to inform practitioners and researchers about the current knowledge, challenges and developments of relevance to women's mental health.

This themed issue brings together cutting-edge perspectives, empirical findings and conceptual advancements that aim to fill critical gaps in knowledge on the influence of oestrogens and progestagens on women's mental health. A central focus is sensitivity to gonadal steroid variations as a primary driver of mental conditions occurring or being exacerbated during periods of hormonal flux, an emerging diagnostic factor that requires greater attention and care.^{1,2} The broad lack of consideration for the impact of ovarian hormones, and their neurosteroid metabolites, on mental health has indeed contributed to the categorisation of certain conditions – such as premenstrual dysphoric disorder (PMDD), menopausal depression and peripartum mood disorders – as understudied, missed or misdiagnosed psychiatric syndromes. This collection supplants a lack of hormone-informed psychiatric frameworks.

Across a woman's life, hormonal transitions shape the brain in profound ways – each phase bringing its own neurobiological shifts and vulnerabilities. We begin our journey by considering the

pubertal ovarian hormone flux in the brain of girls. Clinically, this can be a time of increased risk of mental illness onset, with rapidly fluctuating and altering presentations of a variety of conditions. In adolescence, neuroendocrine processes triggering puberty begin before many outward signs of physical maturation are visible. The tempo and timing of hormonal changes begin activating the brain circuits involved in emotion regulation and mental health. Recent findings reveal how these dynamics intersect with emerging risks for depression, psychotic experiences and other forms of psychopathology.³ Neuroimaging studies add another layer, showing that the adolescent brain organises itself differently by sex – insights made possible by personalised brain atlases that trace individual functional networks. Together, these discoveries deepen our understanding of why girls face a higher risk for anxiety and depression during this critical transition.

As the narrative moves forward, comorbidities come into view. Studies in this issue examine the frequent co-occurrence of premenstrual symptoms not only with mood disorders but also with attention-deficit hyperactivity disorder. Whether these conditions emerge independently or sequentially, the overlap highlights a pressing need for more tailored clinical and biological insights – in particular to guide treatment for individuals facing multiple challenges.

Premenstrual dysphoric disorder is further explored through the lens of stress response and exposure to stressful life events. Similarly, polycystic ovary syndrome – typically viewed as an endocrine condition – emerges as a disorder with psychiatric implications, influencing mood and vulnerability to mental health issues. This underscores the importance of integrating brain and behavioural perspectives in hormonal health research.

As the life journey continues for the young woman, the perinatal time brings new challenges for some, with the impact of ovarian hormones in the central nervous system. Pregnancy and postpartum indeed represent other critical windows of vulnerability. Research featured here investigates how women with premenstrual mood sensitivity may follow identifiable trajectories of depressive symptoms during the perinatal period. These patterns suggest that sensitivity to ovarian hormones could be a marker for risk, pointing to the promise of early identification and preventive care.⁴ Some studies highlight the benefits of improved phenotyping and integrated mental health screenings within paediatric settings,⁴ while others emphasise the role of

antidepressant timing and genetic predispositions in shaping treatment responses during postpartum.



In the third stage of her reproductive hormone journey, the woman begins the menopause transition where fluctuating ovarian hormones impact the brain, creating a 'bookend'-like effect to the changes seen in puberty to some extent. Menopause, too, is a turning point whose impact stretches across cognitive, emotional and neurodegenerative domains. Contributions in this issue reveal how different menopause subtypes and hormone therapy strategies affect mental health in midlife. The clinical trial testing transdermal oestradiol or testosterone provides a glimpse into promising interventions for menopausal depression. Nevertheless, alongside these advances, the field grapples with inconsistent terminology and a lack of training in menopause care, which continue to limit both clinical progress and research efforts.⁵

Furthermore, this issue tackles methodological challenges in assessing the psychiatric effects of hormonal contraceptives.⁶ There is need to better account for individual differences in hormonal sensitivity and subjective experiences – particularly in how stress and mood are processed under the influence of synthetic hormones whose central nervous system effects can be disparate from their naturally occurring counterparts.⁷ Moreover, a refined approach in preclinical research is deemed necessary to develop translationally relevant animal models of perinatal depression and menopausal hormone therapy.

This issue also turns its focus toward discovery – highlighting the ongoing search for biomarkers that could transform how we detect and treat reproductive mood disorders. Spanning genetics, epigenetics and neuroimaging, these investigations aim to usher in an era of precision psychiatry. At the heart of it all is a deeper recognition of how reproductive events shape women's mental and brain health across the lifespan. Encouragingly, a wave of therapeutic breakthroughs is beginning to translate this science into action.⁸ From neurosteroid-based treatments for postpartum depression to hormone-modulating drugs for PMDD, a biologically informed, sex-specific psychiatry is beginning to take form – offering new hope for tailored, effective care.

By integrating findings across the reproductive lifespan, from puberty to menopause, this collection of research reinforces the urgent need for hormone-informed psychiatric care – ensuring that women's mental and brain health is no longer an overlooked aspect of neuroscience but a fundamental pillar of psychiatric and medical research.⁹ This means advancing knowledge that genuinely reflects the value of mental science – knowledge that is essential for evidence-based care.

This themed issue, titled 'Psychiatric symptoms on the ovarian hormone roller-coaster', invites readers to understand how hormonal transitions shape mental health across the lifespan and identify gaps in research and care. Through this collection, we aim to foster a shift in perspective – one that acknowledges the intersection of endocrinology, psychiatry and neuroscience while advocating for precision medicine approaches tailored to women's unique mental health needs. These new perspectives aim to inform better support, policy changes and a deeper understanding of women's mental health, to inspire the implementation of destigmatising, holistic sex-specific care.

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Note

In this themed issue, we use the term 'woman' primarily in reference to individuals assigned female at birth, because the included studies focus on biological processes such as ovarian hormone fluctuations. However, we recognise that hormonal influences on mental health are not confined to those who identify as women, and we acknowledge the importance of expanding research to include individuals across the gender spectrum who may experience hormonal changes due to biology or medical interventions.

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