https://doi.org/10.1038/s41591-025-03879-1

Why menstrual cycle irregularities belong in brain research

Carina Heller, Erynn Christensen, Elle M. Murata, Nicole Petersen, Kathleen Casto, Shae Datta, Bart Larsen & Hector Arciniega

The menstrual cycle requires tight orchestration between the brain and body, and irregularities can be both the cause and the consequence of wide-ranging health issues. Embracing this complexity, instead of excluding individuals with irregular menstrual patterns from research, could reveal novel brain–body interactions, advance neuroscience and improve health outcomes for those affected.

Hormonal fluctuations across the menstrual cycle profoundly shape brain function and structure[1]. Increasingly, clinicians and researchers recognize the menstrual cycle as a key indicator of health status and risk for disease, a 'vital sign', underscoring its relevance to both physical and mental well-being[2]. Menstrual cycle irregularity, whether in length, frequency or severity of occurrence (Box 1), is highly prevalent in humans, affecting nearly one in six female individuals, with some estimates as high as 36%, depending on other risk factors[3]. However, individuals with irregular menstrual cycles are routinely excluded from neuroendocrine brain research studies, leading to a limited and incomplete understanding of brain–hormone interactions. This systematic omission neglects a population frequently burdened by adverse health outcomes, including a higher risk of premature death[4].

Menstrual health is regulated at the nexus of the hypothalamic–pituitary–gonadal (HPG) axis, integrating brain and body systems (Fig. 1). Menstrual cycle irregularities are not merely confounding noise; they reflect distinct endocrine rhythms, neurobiological pathways and an avenue for understanding sex-specific brain health. Importantly, the implications extend beyond neuroendocrine research: menstrual cycle irregularities often co-occur with physical and mental health conditions that are central to many areas of neuroscience, making them an overlooked source of insight.

Here we call for dedicated research efforts into atypical menstrual cycle patterns in neuroimaging and clinical research. We explore emerging findings that reveal the bidirectional relationship between menstrual cycle irregularities and brain function, and we outline how embracing this complexity can inform more precise, personalized approaches to women's health. Addressing this research gap is not just an equity issue; it is essential to advancing the science of brain–body interactions.

Early indicators of systemic health disruptions

Menstrual irregularities are not merely reproductive anomalies; they often serve as key clinical indicators of broader disruptions across endocrine, metabolic and neural systems. Behaviors such as restrictive eating, excessive physical activity and psychosocial stress are strongly associated with disruptions to menstrual cycle patterns[5], with cycle cessation or shortening frequently serving as an early sign of physiological strain. In many cases, a persistent emerging pattern of irregular menstruation is the first observable symptom of an underlying condition, such as a thyroid disorder, polycystic ovary syndrome (PCOS) or endometriosis, all of which are increasingly recognized for their impact on brain structure, function and mental health[6–8]. Furthermore, dysmenorrhea (painful menstrual periods) is strongly linked to (pelvic and non-pelvic) chronic pain and associated brain-imaging findings[9].

However, research is scarce because these conditions have been overlooked for decades. Recognizing menstrual cycle irregularities as meaningful clinical signals creates a critical opportunity for early intervention in disrupted body systems. At the same time, this recognition must be balanced with caution to avoid over-pathologizing menstrual variation, as intra-individual variability in factors such as the length of time between menstrual periods is common in healthy individuals. Further, many individuals with conditions such as PCOS live healthy and fulfilling lives with appropriate support and care.

Irregular menstrual cycles and brain health

Neuroimaging studies have observed complex and dynamic fluctuations in both brain structure and brain function across the regular menstrual cycle, including changes in gray matter volume and thickness,

BOX 1

Irregular menstrual cycles

The term 'irregular menstrual cycles' refers to persistent deviations, in cycle length or menstrual flow, from what is considered a typical cycle. Although there is no consensus on a precise definition, irregular cycles generally fall outside the commonly cited range of 25–30 days (median, 28 days). These irregularities may manifest as amenorrhea (absence of menstruation), oligomenorrhea (infrequent menstruation), polymenorrhea (frequent menstruation) or abnormal bleeding patterns. Contributing factors can include hormonal imbalances, stress, lifestyle factors, certain medications and underlying health conditions such as PCOS, endometriosis or thyroid disorders. Given the diverse causes and presentations, individualized assessment and management are crucial. Further research into the precise characterization, consensus definitions and the clinical importance of irregular cycles is needed to enhance the ability to monitor and manage menstrual health, ultimately improving outcomes for individuals with menstruation-related neurological conditions.

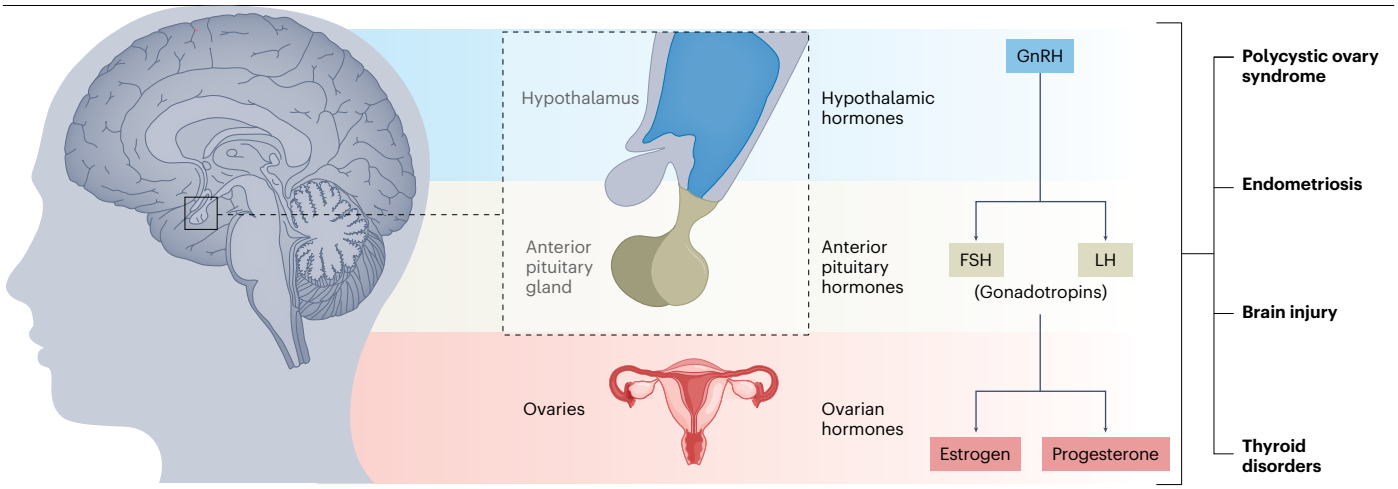

Fig. 1 | The female HPG axis and potential disruptions. The HPG axis guides the rhythmic production of gonadotropins and sex hormones across the menstrual cycle. The hypothalamus signals to the anterior pituitary gland via gonadotropin-releasing hormone (GnRH) to release the gonadotropins luteinizing hormone (LH) and follicle-stimulating hormone (FSH), which trigger the production of estrogen and progesterone from the ovaries. Dysregulation of this tightly coordinated axis is seen in polycystic ovary syndrome (PCOS), endometriosis and thyroid disorders and is also suggested to occur in brain injury.

functional network organization, neural reactivity to stimuli and brain chemistry. These neural shifts closely track cyclical patterns of ovarian hormones, such as pre-ovulatory estradiol peaks and post-ovulatory progesterone surges[1]. By contrast, individuals with irregular cycles often lack these predictable hormonal rhythms because of disruptions in the HPG axis (Fig. 1). Endocrine disorders such as PCOS, endometriosis and thyroid dysfunction can disrupt the balance of estrogen, progesterone and androgens, potentially leading to distinct alterations in brain architecture and function.

Despite growing interest in the brain–endocrine relationship and convincing preliminary evidence that irregular menstrual cycles shape brain functional and structural dynamics in unique ways, individuals with menstrual cycle irregularities remain chronically under-represented in research. Although their exclusion is often justified as a means for minimizing hormonal variability, it introduces a sampling bias, one that sidelines a substantial proportion of the population and limits insight into the full spectrum of menstrual cycle physiology and its effects on the brain.

Neuropsychiatric disorders and the menstrual cycle

The menstrual cycle is governed by a complex neuroendocrine feedback loop between the brain and body. As such, brain health not only is influenced by hormones but also plays a central role in regulating them. Psychiatric conditions such as premenstrual dysphoric disorder (PMDD) and postpartum depression are causally linked to fluctuations in sex hormones. Exacerbations of menstrual cycle-related symptoms have also been observed for mental health conditions characterized by psychosis, mania, depression and substance use[10]. Notably, the incidence of many mental health disorders, such as depression, increases during puberty[11] — a developmental period that also marks the onset of menarche, which is often followed by up to 2 years of irregular menstrual cycles — suggestive of a potential link between early hormonal instability and emerging psychiatric vulnerability.

Furthermore, higher rates of psychiatric comorbidities have been reported in women with menstrual disorders. The reason for such associations remains unknown. Symptoms of prevalent neurological conditions, including epilepsy, movement disorders, migraine, stroke and multiple sclerosis, are all influenced by menstrual cycle phases (or their elimination by hormonal contraceptives). Individuals with these listed conditions report menstrual disorders more commonly compared with individuals without these conditions[12].

Concussion as a lens into brain–menstrual cycle reciprocity

A growing field of research that has provided some early insight into the bidirectional relationship between menstrual irregularities and brain health is brain injury. Concussions have emerged as a substantial disruptor of menstrual cycle regularity. Female individuals who sustain a concussion are at an increased risk of developing menstrual cycle disturbances, including delayed cycles, missed periods and complete amenorrhea[13]. These effects can persist for months after injury, reflecting long-term perturbations in neuroendocrine function. Rather than being peripheral symptoms, these disruptions may be physiological signals of central nervous system strain.

This physiological response may parallel the temporary cessation of menstruation seen in the postpartum period, an evolutionary adaptation whereby elevated prolactin levels suppress ovulation and menstruation, allowing the body to allocate resources toward lactation and infant care. Similarly, in the context of concussion, menstrual disruptions may reflect a reallocation of physiological resources toward neurological repair and survival.

The influence of the menstrual cycle on brain injury outcomes is equally compelling. Hormonal fluctuations may shape both vulnerability to concussion severity and recovery trajectories. For example, concussions sustained during the luteal phase — when progesterone is elevated — are associated with more-severe symptoms and prolonged recovery than those that occur during the follicular phase. These findings implicate the HPG axis in modulating post-injury outcomes[14], emphasizing that concussion recovery is shaped not only by biomechanical factors but also by hormonal state. Additionally, hormonal contraceptive use may mitigate some of these effects by stabilizing hormone levels and supporting recovery[15].

Just as concussions can disrupt menstrual patterns, pre-existing hormonal conditions such as PCOS or endometriosis may shape how individuals experience and recover from brain injury. In contrast, male individuals lack a similarly visible, cyclic biomarker of hormonal disruption, which highlights the unique potential of menstrual health as a window into neuroendocrine function in female individuals. Findings from concussion research illustrate the delicate balance between the brain and endocrine system as an indicator of overall health, underscoring the need for personalized brain-injury management.

Future directions and implications for clinical practice

Advancing the science of menstrual cycle irregularities and brain health will require interdisciplinary collaboration and innovative research design. Longitudinal studies that integrate neuroimaging, endocrine profiling and comprehensive health assessments will be critical to elucidating the mechanisms that link menstrual disruptions to neurological outcomes. Large-scale epidemiological studies, particularly those that include racially, socioeconomically and hormonally diverse populations, are also needed to capture the full spectrum of menstrual variability. Importantly, reproductive health must be assessed using standardized, validated tools that allow consistent characterization of cycle patterns across studies and clinical settings.

In clinical practice, greater awareness of the neurological implications of menstrual cycle irregularities is urgently needed. Routine integration of cycle tracking and reproductive history into health assessments could facilitate the early detection of endocrine or neurobiological dysfunction and mental health conditions, enabling timely intervention. Hormonal contraceptives, widely used for both health and lifestyle reasons, complicate this landscape. Although they are essential for many individuals, these medications can obscure symptoms of underlying conditions, such as PCOS, endometriosis or thyroid dysfunction, particularly when initiated during adolescence, before the emergence of overt reproductive pathology. Understanding how hormonal contraceptives affect the brain remains an important frontier. These medications directly alter the hormonal milieu that shapes mood, cognition and neuroplasticity, yet their neurobiological impact remains understudied.

A precision medicine approach that considers individual hormonal profiles, reproductive history and neurological vulnerabilities will be essential for tailoring treatment and supporting cognitive and emotional health in those with menstrual-related conditions. Finally, dismantling the stigma surrounding menstruation and menstrual cycle irregularities is critical. Promoting open, inclusive dialogue empowers individuals to seek care and advocate for their health. By addressing cultural barriers and clinical blind spots, we can ensure that reproductive physiology is recognized not as a niche concern but as a fundamental aspect of comprehensive, evidence-based healthcare for all.

Advancing the understanding of brain–hormone interactions in the context of menstrual irregularities may also lay the groundwork for broader insights into how hormonal fluctuations — whether diurnal, seasonal or lifestyle driven — shape brain function and structure across sexes and life stages. The implications of this work thus extend well beyond reproductive health, offering a roadmap for future research on the endocrine foundations of brain health more broadly.

Conclusion

The dynamic, bidirectional relationship between menstrual cycles and brain health demands a more integrated, biologically informed approach to research and clinical care. Menstrual irregularities are not peripheral concerns; they are neuroendocrine signals that may reflect, and contribute to, broader disruptions in brain function and resilience. Addressing this intersection requires dismantling of methodological exclusions, embracing of menstrual cycle variability in scientific inquiry and fostering of interdisciplinary collaboration. With the integration of advanced neuroimaging, longitudinal hormonal profiling and inclusive clinical frameworks, the full spectrum of menstrual cycle–brain interactions can begin to be uncovered. These insights will pave the way for more personalized and equitable care, recognizing the menstrual cycle not only as a reproductive metric but also as a vital sign of neurological health.

Carina Heller [1,2,3,4] ✉, Erynn Christensen[5], Elle M. Murata[3], Nicole Petersen[6], Kathleen Casto [7], Shae Datta[8,9], Bart Larsen[1,2] & Hector Arciniega [9,10]

[1]Masonic Institute for the Developing Brain, Institute of Child Development, University of Minnesota, Minneapolis, MN, USA. [2]Department of Pediatrics, University of Minnesota, Minneapolis, MN, USA. [3]Department of Psychological and Brain Sciences, University of California, Santa Barbara, CA, USA. [4]Department of Psychiatry and Psychotherapy, Jena University Hospital, Jena, Germany. [5]Institute of Behavioral Sciences, Feinstein Institutes for Medical Research, Manhasset, NY, USA. [6]Department of Psychiatry & Biobehavioral Sciences, University of California, Los Angeles, Los Angeles, CA, USA. [7]Kent State University, Department of Psychological Sciences, Kent, OH, USA. [8]Department of Neurology, NYU Grossman School of Medicine, New York, NY, USA. [9]NYU Langone Concussion Center, NYU Langone Health, New York, NY, USA. [10]Department of Rehabilitation Medicine, NYU Grossman School of Medicine, New York, NY, USA.
✉e-mail: cheller@umn.edu

Published online: 13 August 2025

References

1. Dubol, M. et al. *Front. Neuroendocrinol.* **60**, (2021).
2. Vollmar, A. K. R., Mahalingaiah, S. & Jukic, A. M. *Fertil. Steril. Rev.* **6**, 100081 (2025).
3. Kwak, Y., Kim, Y. & Baek, K. A. *PLoS ONE* **14**, 1–12 (2019).
4. Wang, Y. X. et al. *BMJ* **371**, m3464 (2020).
5. Huhmann, K. *Clin. Ther.* **42**, 401–407 (2020).
6. Pinto, J., Cera, N. & Pignatelli, D. *J. Endocrinol. Invest.* **47**, 1–22 (2024).
7. Chambers, T. et al. *J. Clin. Endocrinol. Metab.* **106**, 688–696 (2021).
8. Maulitz, L. et al. *Front. Neuroendocrinol.* **65**, 100988 (2022).
9. Li, R. et al. *Am. J. Obstet. Gynecol.* **223**, 350–371 (2020).
10. Handy, A. B., Greenfield, S. F., Yonkers, K. A. & Payne, L. A. *Harv. Rev. Psychiatry* **30**, 100–117 (2022).
11. ACOG Committee. *Obstetrics Gynecol.* **130**, e32–e41 (2017).
12. Roeder, H. J. & Leira, E. C. *Curr. Neurol. Neurosci. Rep.* **21**, 34 (2021).
13. Snook, M. L., Henry, L. C., Sanfilippo, J. S., Zeleznik, A. J. & Kontos, A. P. *JAMA Pediatr.* **171**, 879–886 (2017).
14. Agha, A. & Thompson, C. J. *Clin. Endocrinol. (Oxf.)* **64**, 481–488 (2006).
15. Wunderle, K., Hoeger, K. M., Wasserman, E. & Bazarian, J. J. *J. Head Trauma Rehabil.* **29**, E1–E8 (2014).

Acknowledgements

C.H. is supported by the German Research Foundation (grant 544183227). E.C. is supported by Northwell Health Advancing Women in Science and Medicine (Career Development Award). B.L. is supported by the US National Institutes of Health (R00MH127293). H.A. is supported by the US National Institutes of Health (R21NS140565), the National Institute on Minority Health and Health Disparities Loan Repayment Program (L32MD016519), an Alzheimer's Association grant (25AARG-NTF-1377286) and the Burroughs Wellcome Fund Postdoctoral Diversity Enrichment Program.

Author contributions

C.H. was responsible for conceptualization, visualization and writing — original draft. E.C. and H.A. contributed to conceptualization and writing — review and editing. E.M.M. contributed to visualization and writing — review and editing. N.P., K.C., S.D. and B.L. contributed to writing — review and editing.

Competing interests

The authors declare no competing interests.