

# Menstruation – The female research advantage

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**While funding organizations are increasingly mandating equal representation of sexes and genders in research, hormonal fluctuations are still often viewed as complicating factors.**

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**Professor Belinda Pletzer argues for a shift in perspective, suggesting that the menstrual cycle should not be seen solely as a complicating factor, but as one of many variables influencing research**

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Historically, the menstrual cycle has disadvantaged women from a research perspective. Since it was unclear to what extent the hormonal fluctuations along the menstrual cycle affected brain and body functions, women were perceived as too complicated to study due to potential female ‘instability’ in variables of interest. This has, among other factors, like safety concerns for potential pregnancies in women of childbearing age, led to research studies focusing exclusively on male samples. <sup>(1)</sup>

As a result, we are now facing a massive gender data gap, from preclinical animal work to basic neuroscience and clinical care. Many psychological and neuroscientific models were developed on male participants, and simply transferring them to female samples has proven challenging. <sup>(2)</sup> However, it is even more problematic when diagnostic guidelines fail to capture how disorders typically manifest in women <sup>(3)</sup> or when common treatment options are less suitable for female patients.

**Women are more ‘stable’ than we think!**

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Considering the menstrual cycle in research studies is not only important, it is crucial. Certain variables, such as brain connectivity, are heavily influenced by ovarian hormones. <sup>(5)</sup> However, two decades of menstrual cycle research have also identified many variables for which menstrual cycle changes are only small – e.g., brain structure <sup>(5)</sup> – or negligible on average. For example, we observed that many cognitive tasks do not show changes along the menstrual cycle <sup>(6)</sup> or across pill phases <sup>(7)</sup> – so hold off on cycle-based scheduling of exams for now! Likewise, mood changes along the menstrual cycle are highly individualized, with only a fraction of women presenting with premenstrual disturbances but no changes in the majority of women. <sup>(8)</sup>

We suspect that behind this outward stability lies a complex information-processing system operating continuously in the background, working hard to maintain functional balance during periods of change, such as hormonal fluctuations along the menstrual cycle. We repeatedly observed brain changes during the menstrual cycle in verbal and spatial tasks, while performance remained consistent across all cycle phases. <sup>(9)</sup> Brain

connectivity measures reflect part of this system and, therefore, show stronger changes throughout the menstrual cycle than the behavioural parameters they support. Thus, if we study parameters reflecting neuroplasticity, menstrual cycle phase is an important parameter to control. However, there are many research designs for which controlling the menstrual cycle may be less important than controlling for other hormonally mediated variables, such as stress, sleep, or time of day. Thus, rather than viewing the menstrual cycle as the one thing that immeasurably complicates female research subjects, we should consider it as one of many factors potentially contributing to intra-individual variability.

## **Men are less ‘stable’ than we think!**

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Among these factors are various hormonal systems that exhibit circadian, ultradian, or infradian variability in both males and females. However, even when focusing on reproductive hormones, women are not the only ones experiencing fluctuations. It is well-documented that male testosterone changes throughout the day and exhibits seasonal variability.<sup>(10)</sup> However, there is also evidence that changes in testosterone levels do occur from day to day, and most importantly, they are linked to cognition.<sup>(10, 11)</sup> Thus, accounting for intra-individual fluctuations in testosterone may be equally important as accounting for the menstrual cycle, or even more so, when examining the behavioural level. Thus, the common research practice of using men as a default due to presumed stability is flawed. Because stability is not the default, change is. Without the capacity for change, we lack adaptability to environmental challenges. Thus, a plethora of biological rhythms ensures the brain’s adaptability to change in all sexes and genders.

Unfortunately, we do not know as much about day-to-day fluctuations in testosterone as we do about the menstrual cycle – specifically, we do not know how to time them. Knowing whether testosterone levels are high or low requires measuring them daily, which is not always feasible or affordable. Lacking a reliable external marker for reproductive hormone changes makes the research process more complicated in men.

## **Menstruation helps research timing**

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In contrast, while we do not yet know the full extent of variables affected by the menstrual cycle, we know how to study it. Menstruation is one of the many tools we have to assess hormonal status in women. So, whatever one’s personal experiences with menstruation may be – as researchers we must appreciate it because it is an objectifiable outwards sign that one of the many internal rhythms potentially relating to our research findings has been reset. If we view menstruation as an asset rather than a liability, inclusivity in research follows in course. In recognizing that hormonal changes go beyond the menstrual cycle and concern everyone, rather than excluding the female sex, menstruation provides a strong argument for their inclusion. Because menstruation helps us time an internal rhythm – and it does so exclusively in females.

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3. Garb, 2021: <https://doi.org/10.1016/j.cpr.2021.102087>
4. NHLBI Policy for the Inclusion of Women, Minorities, and Participants Across the Lifespan in Clinical Research | NHLBI, NIH
5. Pletzer et al., 2025: <https://doi.org/10.1016/B978-0-12-820480-1.00151-0>
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