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# Evolution, the Menstrual Cycle, and Theoretical Overreach

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## Abstract

A considerable body of recent psychological research has attributed a variety of menstrual cycle-related changes in social behavior to evolutionarily adaptive functions. Although these studies often draw interesting and unusual conclusions about female emotion and behavior within evolutionary theory, there are significant limitations to these studies that have not been addressed in this literature. In the present paper, we outline several methodological and conceptual issues related to the menstrual cycle that constitute threats to the internal validity and theoretical integrity of these studies. Throughout the paper we recommend specific guidelines to address these issues, and we emphasize the need to apply more comprehensive and sophisticated theoretical structures when considering menstrual-cycle related changes in emotion and behavior.

Over the last fifteen years, a significant number of published studies have examined menstrual cycle-related changes in behaviors that are not explicitly reproductive. Although the target variables of these studies have differed significantly, including voting tendencies (Durante, Rae, & Griskevicius, 2013), intra-sex dehumanization (Piccoli, Foroni, & Carnaghi, 2013), and tips earned by lap dancers (as a proxy for changes in fertility cues expressed by the performer; Miller, Tybur, & Jordan, 2007), the common theoretical goal has been to provide an evolutionary explanation for behaviors that appear to fluctuate across the menstrual cycle. (For the sake of simplicity, the term *behavior* is used for all phenotypes discussed, although some would not typically be called behaviors). However, a failure to consider the complexity and interdependent dynamics of the many biological, psychological, and social changes of the menstrual cycle significantly limits the conclusions that can be drawn from these studies. Moreover, it is neither necessary nor justified to apply an evolutionary explanation for all observed menstrual cycle-related behavioral phenotypes.

Our objections are not with evolutionary theory *per se*. Surely, most biological aspects of the menstrual cycle have evolved for some important function, and observed psychological changes will in some way depend on those biological changes (including changes in CNS function). Our primary concerns, rather, lie with *(1)* the lack of attention to the many other

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menstrual cycle-related symptoms that may result in third-variable confounds and compromised internal validity; *(2)* the exclusive focus on proximity to ovulation as the driving force of cyclical changes in behavior, rather than balanced attention to both ovulation and menstruation; *(3)* the lack of attention to individual differences; and *(4)* reliance on theoretical models that fail to consider or specify pathways involving the many biological, physical, psychological, and social changes that are associated with the menstrual cycle. Therefore, in the present paper we will argue that these studies have not provided sufficient empirical evidence to demonstrate that the targeted behaviors have *evolutionarily adaptive functions*, and that a simple temporal correlation between a behavioral phenotype and the menstrual cycle does not imply an evolutionarily adaptive function for that behavioral phenotype.

Note that the goal of the current paper is not to present an alternative theory attempting to attribute evolutionarily adaptive functions to menstrual cycle-related changes in social behavior. Given the extreme heterogeneity of the target behaviors examined in this literature, it is very unlikely that any single theory could accomplish this. In fact, studies in this area often drawn on different theoretical concepts from within of evolutionary psychology. Rather, our goal is to argue that certain methodological and conceptual limitations consistently threaten the internal validity and theoretical integrity of studies in this area.

Note also that the focus of the current paper is not on the reliability/replicability of specific effects. Therefore, concerns raised in the current paper are not applicable to those studies or areas of research that do not replicate and that may eventually be regarded as non-effects. Thus, the issues raised here are germane only as long as there are reliable effects for which internal validity could be questioned.

This paper is organized into the following two main sections: methodological issues specifically related to research on the menstrual cycle, and conceptual issues underlying the attribution of menstrual cycle-related changes to evolutionarily adaptive functions.

## Methodological Issues

A typical menstrual cycle is about 28 days, and can be divided roughly into two halves, bisected by ovulation. The first half - from menses to ovulation - is the follicular phase, and is characterized by low progesterone and increasing estradiol, with a primary estradiol peak just prior to ovulation. The second half - from ovulation to the next menses - is the luteal phase, and is characterized by high levels of progesterone and a secondary and slower peak in estradiol. Estradiol and progesterone fall precipitously just prior to and during the first few days of menses, and the cycle begins again. Historically, the fields of behavioral neuroscience and psychiatry have examined how cyclical changes in behavior are driven by these steroid dynamics.

Alternatively, in evolutionary psychology studies, the menstrual cycle is typically conceptualized unidimensionally in terms of *proximity to ovulation,* with the goal of identifying high fertility days that are temporally close to ovulation, and low fertility days that are temporally distant from ovulation (i.e., perimenstruum, which includes those days

immediately prior to and during menstruation). In many cases, epidemiological data are used to estimate the probability of conception (given intercourse) on a given day of the cycle. In many of these studies, a *between-subjects design* is used to examine the effects of the menstrual cycle, with some women participating on a high fertility day (i.e., high conception probability due to close proximity to ovulation), and others participating on a low fertility day (i.e., low conception probability due to greater distance from ovulation). Analyses then focus on main effects of cycle-phase regarding a single or limited number of dependent variables, assuming a homogeneous effect across women. Unfortunately, these methods come with significant limitations to internal validity.

In the paragraphs that follow, we discuss three critical omissions that are characteristic of this literature: *(1)* failure to consider the staggering array of physiologically-driven changes that occur *throughout the body and across the menstrual cycle* (see Farage, Neill, & MacLean, 2009, for review); *(2)* failure to consider and discuss analytic similarity/equivalence between *proximity to ovulation* and *proximity to menstruation;* and *(3)* failure to consider the overwhelming evidence for significant *individual differences* in these menstrual cycle changes across women. This section concludes with a discussion regarding the distinction between *functional proximal causes* and *third-variable confounds*.

## Menstrual Cycle-Related Changes Throughout the Body

Although ovulation and menstruation are key signposts that mark critical transition points in the monthly reproductive cycle, these events are only two of the many physiological, psychological, and physical changes that unfold across the cycle. Moreover, in contrast to the solitary focus on ovulatory and high-fertility days found in the evolutionary literature, decades of research have demonstrated that many of the physical and psychological changes of the menstrual cycle occur most markedly in the days prior to and during menstruation (referred to as the *perimenstruum*). For example, observed perimenstrual changes include irritability, anxiety, depression, cognition, back pain, headaches, acne, and cramps, to name just a few (see for example, Bloch, Schmidt, & Rubinow, 1997; Freeman, DeRubeis, & Rickels, 1996; Halbreich, Endicott, Schacht, & Nee, 1982; Hartlage, Freels, Gotman, & Yonkers, 2012; Kiesner & Pastore, 2010; Steiner et al., 2011). Additionally, there are also *less noticeable* physiological changes affecting many systems and functions throughout the body, including, for example, the immune system, the digestive system, the cardiovascular system, and thermoregulation (see, Farage et al., 2009, for a review).

This vast array of changes is relevant to the present discussion because many are capable of directly regulating the specific behaviors examined in the evolutionary literature, and thus could result in third-variable confounds that threaten the internal validity of these studies (the distinction between third-variable confounds and *functional proximal causes* is discussed in a later section). For example, symptoms such as headaches, cramps, irritability, anxiety, and depression may influence how a woman feels about herself (attractiveness, self-esteem) or how she responds to certain characteristics/traits of others, and may therefore influence menstrual cycle-related changes in dress and mate selection (to name only two examples), both of which have been studied in the context of evolutionary models. Thus, whereas research presented in the evolutionary literature has had a solitary focus on

ovulatory and high fertility days as the defining aspect of the menstrual cycle, we emphasize the need to consider the vast array of physical and psychological changes which occur perimenstrually and that may influence observed changes in target behaviors.

To provide specific examples of how these changes could result in third-variable confounds, spurious associations, and poor internal validity, several key examples of potentially confounding symptomatic changes across the menstrual cycle are presented in Table 1. Specifically, this table lists six types of symptoms that are commonly associated with the perimenstruum, as well as some empirically established clues to the underlying physiology of these symptoms. It is important to emphasize the wide range of tissues and physiological processes involved, which is due to the broad distribution of steroid receptors across many tissues, regulating the expression of many tissue-specific genes, and demonstrating very different functions across cell types (see, Farage et al., 2009). Most importantly for the present discussion is the third column, which lists possible behavioral or psychological covariates of these symptoms. Put simply, these symptoms and behavioral/psychological covariates represent uncontrolled confounds of target behaviors in evolutionary research. For example, menstrual cycle-related headaches and migraines could influence changes in mood, physical activity, social withdrawal, and sexual interest, which in turn could influence evolutionarily relevant target variables such as mate selection or clothing preference.

It is important to note that associations between menstrual cycle-related physical and psychological symptoms are well-established in the literature (e.g., Kiesner, Mendle, Eisenlohr-Moul, & Pastore, 2016). Moreover, research has also demonstrated associations between menstrual cycle-related symptoms and changes in daily activities such as work (Borenstein, Dean, Leifke, Korner, & Yonkers, 2007; Halbreich, Borenstein, Pearlstein, & Kahn, 2003; Robinson & Swindle, 2000), sports (Hillen, Grbavac, Johnston, Straton, & Keogh, 1999; van Iersel, Kiesner, Pastore, & Scholte, 2016), and social activities and relationships (Halbreich et al., 2003; Robinson & Swindle, 2000; van Iersel et al., 2016), as well as changes in body-image dissatisfaction (Altabe & Thompson, 1990; Carr-Nangle, Johnson, Bergeron, & Nangle, 1994). Additionally, Kiesner (2017) has provided a detailed analysis of how menstrual cycle-related symptoms may interfere with important daily and developmental tasks during adolescence. Thus, although some of the specific confounding effects listed in Table 1 are hypothetical, there is strong evidence that these confounds exist, and strong theoretical motivation to suspect that they create important confounds and biases in the research considered in the current paper.

To underline the extent to which these confounds have been ignored in this area of research we examined all published papers used in two recent meta-analyses of studies testing for changes in women's mate preference across the menstrual cycle (Gildersleeve, Haselton, & Fales, 2014a; Wood, Kressel, Joshi, & Louie, 2014; published papers as indicated by an asterisk in the reference list of these meta-analyses). Based on a thorough review of the introductions, methods, results, discussions, tables, and figures, of all 50 of the published papers included in these meta-analyses (some with multiple studies), we found that *none of the papers controlled for these physical or psychological confounds, and only 3 papers mentioned perimenstrual symptoms*, all 3 giving only cursory mention to these changes in their discussions. Moreover, potential confounds caused by perimenstrual symptoms/

changes were not mentioned (1) in either of the meta-analyses; (2) in either of two critiques of the Gildersleeve et al., meta-analysis (Harris, Pashler, & Mickes, 2014; Wood & Carden, 2014) or in the response to those critiques (Gildersleeve, Haselton, & Fales, 2014b). Note that Harris (2011; included in both meta-analyses) did attempt to control for menstrual cycle-related changes in mood, although because no effect was found the editor requested that the measure of mood be removed from the final paper (personal communication). Thus, with only one known exception, it is clear that these important confounds are *not* considered in this area of research.

These unmeasured confounds also limit the utility of measuring ovarian steroids across the menstrual cycle with the hopes of demonstrating that steroids are the proximal causal *mechanism* for menstrual cycle-related behavior change (for examples of this approach see, Roney & Simmons, 2008, 2013; Welling et al., 2007). Specifically, although behavioral changes associated with the menstrual cycle *could* be expected to covary with steroid levels, this temporal covariation cannot be interpreted as demonstrating a proximal causal mechanism. This is because a behavioral change that covaries with steroid levels could easily be explained (i.e., mediated) by the effects of steroid changes on the many other physical and psychological changes/symptoms described above (e.g., steroid changes ➔ headaches/cramps ➔ changes in social behavior). Thus, an association between steroid and behavior, without considering the intervening effects of headaches/cramps, would lead to invalid conclusions of putative cause. Moreover, steroid *levels* do not capture the highly complex set of effects associated with steroid change, lagged effects, and dependency of effects on duration of tonic levels (see for example, Schmidt et al., 1991; Schmidt, Nieman, Danaceau, Adams, & Rubinow, 1998; Somerville, 1975). Thus, although studies that include steroid measures (even measuring multiple steroids) add some information regarding timing of steroid changes, magnitude of those changes, and whether ovulation actually occurred, in the absence of adequate controls for a wide range of physiological, psychological, and physical changes, steroid measures do not demonstrate that steroids are the proximal causal *mechanism (direct hormonal effects on social behaviors)* that authors hope to find.

Thus, the basic methodological problem is a simple *third variable confound* threatening the internal validity of these studies - but in this case, there is a staggering array of third variables that could result in an association between the menstrual cycle and change in the target behaviors (see Table 1). Excluding these many menstrual cycle-related changes, either from the theoretical framework or analytically, is to assume that these changes have no effect on the target variables. As a result, alternative explanations go untested, and typically these confounds are not even discussed as critical weaknesses.

To address this ubiquitous omission we recommend a simple guideline requiring that all studies in this area either (1) control for a common set of physical and psychological symptoms of the menstrual cycle (see for example, Endicott, Nee, & Harrison, 2006; Freeman et al., 1996, for PMS/PMDD assessment tools); or (2) provide an explicit discussion explaining why these symptoms do not present threats to the study's internal validity. This approach would be consistent with, and no more burdensome than, well-established guidelines requiring that studies control for gender, S.E.S., or age (depending on the area of research), when those variables could potentially influence the outcome. Lists of

common symptoms are easily found (as noted above), but as a very simple starting point one could refer to the DSM-5 criteria for PMDD (APA, 2013).

## Proximity to Ovulation vs. Proximity to Menstruation

For theoretical reasons, research testing evolutionary models of menstrual cycle-related behavior change has focused on *proximity to ovulation* (and the related *conception probability)* as the defining aspect of the menstrual cycle, and the primary causal construct of behavior change. However, it must be recognized that, at an analytic level, *proximity to ovulation* is simply the inverse of *proximity to menstruation*. Therefore, an increase in behavior around ovulation can be statistically modelled as an increase around ovulation *or* as a decrease around menstruation. Alternatively, an increase in behavior around menstruation can be modeled as an increase around menstruation *or* as a decrease around ovulation. Note that, at a statistical level the analytic models testing effects of proximity to ovulation vs proximity to menstruation would be equivocal, and the only things to change would be the direction of the effect (increase vs. decrease) - *and the theoretical interpretation*. Moreover, because many women experience *perimenstrual* changes in physical, psychological, and physiological symptoms, and these changes could influence many types of social behavior, there is a very real risk for third-variable confounds that could create perimenstrual changes in behavior that only appear to be related to ovulation/fertility.

For example, while menstrual headaches may *cause a decrease* in some specific social behaviors during menstruation, this effect could be statistically modeled and interpreted as an *increase* in those social behaviors close to ovulation. However, this increase in social behavior around ovulation would simply reflect a *spurious* correlation that is the *inverse* of the actual causal effect of the menstrual headache - occurring during menstruation. Note that the difference in interpretation and theoretical structure is not trivial and holds vastly different implications for understanding women's menstrual cycle-related changes in behavior. Thus, choosing ovulation over menstruation as the exclusive point of reference inherently leads to a biased interpretation. Although this choice may be theoretically expedient, it is not justified when there is an equally or even more theoretically plausible alternative. Note that our point is not that it is universally preferable to interpret behavior change in relation to the perimenstruum rather than ovulation, but rather that the implications are very different, and one must have strong and theoretically justifiable reasons for choosing one and not choosing the other. At a very minimum, both should be considered.

Note that, because the third-variable confounds and biased interpretations described above depend on changes associated with the *perimenstruum*, it could be hypothesized that excluding premenstrual and/or menstrual days could resolve these problems. However, examining all published papers included in the Gildersleeve et al. (2014a) and Wood et al. (2014) meta-analyses it is clear that there has been no systematic attempt to apply this control. Specifically, of the 50 published studies included in these two meta-analyses, only 16 excluded some premenstrual or menstrual days (or both), with very different days excluded across studies (and only three provided any rational for doing so, see below for further discussion). For example, of these 16 studies, seven excluded some menstrual days,

four excluded some premenstrual days, and five excluded some days from both the premenstrual and menstrual days. Importantly, however, the specific days excluded vary radically across studies (e.g., the entire luteal phase vs. two premenstrual days), a point we will return to in a following paragraph.

Moreover, it must be underlined that even eliminating some premenstrual or menstrual days is not an adequate control for the many changes that occur across the full menstrual cycle that could easily bias the results. For example, studies that exclude premenstrual days (i.e., late luteal phase), create a contrast between fertile days and menstrual days, and because many women experience a variety of symptoms during menstruation, including headaches, cramps, depression, anxiety, and lethargy, this approach does not resolve potential third-variable confounds associated with menstrual-related symptoms. Alternatively, studies that exclude only menstrual days create a contrast between fertile days and premenstrual days, and because many women experience a variety of premenstrual symptoms, including headaches, bloating, acne, and mood changes, this approach also does not resolve the potential for third-variable confounds associated with premenstrual symptoms.

Finally, some studies have excluded both premenstrual and menstrual days. Specifically, as noted above, five of the 50 published studies included in the two meta-analyses took this approach. However, there are three significant problems that limit this approach and how it has been used. First, there is significant heterogeneity in the days that have been excluded and included across these studies. For example, Cárdenas and Harris (2007) targeted their assessment to happen on days 12 and 22 of the cycle, excluding all other days; Eastwick and Finkel (2012) compared five fertile days with nine days during the luteal phase, excluding the last three premenstrual days; Jones, Little, et al., (2005) compared seven fertile days with seven days during the luteal phase, excluding the last four premenstrual days; Provost, Troje and Quinsey (2008) compared three fertile days with three days during the luteal phase, excluding the last four premenstrual days; and Rupp et al. (2009) compared three fertile days with five days of the luteal phase, excluding the last five premenstrual days. Although all of these studies attempt to compare fertile days with some mid-luteal days, excluding some days closest to menstruation (as well as all menstrual days), they all assume (implicitly) that the mid-luteal phase (even up to three days premenstrual), are symptom free. However, this assumption is not supported by the literature, and brings us to the second problem: that many women who experience premenstrual symptoms begin to experience these symptoms very soon after ovulation, and not just during the last 5–7 premenstrual days (Eisenlohr-Moul et al., 2019; Freeman et al., 1996; Pearlstein, Yonkers, Fayyad, & Gillespie, 2005). Finally, the third problem is a lack of any theoretical justification for choosing which days to include and exclude, raising concerns that in some cases the selection of these days may be neither theoretically driven nor chosen prior to data analysis.

Moreover, this lack of theoretical consideration when excluding premenstrual or menstrual days is common across nearly all the studies that have done so. For example, of the 16 studies cited above, that excluded some premenstrual or menstrual days, only 3 studies provided some justification for why specific days were excluded (i.e., to avoid a disgust taboo associated with sex during menstruation that could have influenced the results, Beaulieu, 2007; and to maximize contrast across both fertile and non-fertile days, and across

hormonal states, Jones, Little et al., 2005, and Jones, Perrett et al., 2005 – note that none of these three studies considered possible confounds with perimenstrual symptoms). For the remaining studies, the *unstated* motivation *seems to be* the creation of a purer comparison between fertile vs. non-fertile days, with no agreement regarding which days constitute the relevant non-fertile days, and with no recognition of the implications regarding perimenstrual symptoms associated with the excluded and included days.

A more sophisticated methodological approach would be to consider either the entire cycle during which changes may occur (Kiesner et al., 2016; Mira et al., 1995), or multiple moments of the cycle, such as early and late follicular, ovulatory, and early and late luteal phases, as is commonly done in other literatures concerned with cyclical effects on behavior (Gallant, Popiel, Hoffman, Chakraborty, & Hamilton, 1992; Lester, Keel, & Lipson, 2003; Pearlstein et al., 2005). Thus, rather than focusing on proximity to one point in the cycle (ovulation), more sophisticated approaches are available that consider the menstrual cycle as an actual cycle, with many fluctuating physiological changes, rather than as the distance from a single event. Moreover, as demonstrated by Kiesner et al. (2016), this approach also allows one to simultaneously test for complex associations in the *cyclical change* of many variables (e.g., using SEM).

Overall, the choice to focus on proximity to ovulation rather than proximity to menstruation presents serious threats to the validity of conclusions regarding the putative cause of behavior change. There are clear and documented reasons to hypothesize that perimenstrual symptoms could be driving behavioral changes that only appear to be associated with ovulation. Moreover, past attempts at excluding premenstrual or menstrual days (or both) have lacked theoretical justification, and in any case would not provide the desired control.

Thus, given these concerns, we recommend three specific guidelines to help ensure that analyses and theoretical inferences are sound. First, as discussed above, excluding premenstrual, menstrual, or perimenstrual days as a way of controlling for perimenstrual symptoms provides no clear advantages, is fundamentally misleading, and should therefore be avoided. Second, when possible, studies should measure and model the whole menstrual cycle, rather than discrete moments of the cycle. Finally, analyses and interpretations should be presented in which readers are made aware of alternative interpretations that could be derived if a different temporal point of reference were used. This third point may not require that all data be analyzed twice, considering both proximity to ovulation and proximity to menstruation as points of reference, but at least that a clear rational be provided for selecting one over the other, and that possible alternative interpretations, based on selecting the other temporal point of reference, be provided to readers. These guidelines would help ensure robust and valid conclusions when addressing questions related to the menstrual cycle.

## Individual Differences and Within Person Analyses

Research linking menstrual cycle changes in social behavior with evolutionarily adaptive functions has implicitly taken the position that these cyclical changes in behavior are universal and represent *functional adaptations that are generalizable to all women*. Such a position assumes a high degree of homogeneity in menstrual cycle-related behavioral changes. However, this is incompatible with the bulk of the longitudinal and experimental

evidence on the subject, which demonstrates extreme heterogeneity in hormonal and cyclical effects.

For example, there is impressive variability across women in the specific types of menstrual cycle changes experienced, in the magnitude of changes experienced, and even in the direction of those premenstrual changes (i.e., feeling better or worse; Kiesner, 2011; Kiesner & Martin, 2013; Kiesner et al., 2016; Van Reen & Kiesner, 2016). For example, Figure 1 (from Kiesner et al., 2016) illustrates the robust individual differences in cyclical changes in a variety of symptoms (both physical and psychological), with some women showing increases in symptoms during the perimenstruum, some women showing no detectible cyclical change, and some women showing increases in symptoms during the mid-cycle. Moreover, although *large and clinically severe* levels of perimenstrual symptoms may be the exception rather than the norm (Gehlert, Song, Chang, & Hartlage, 2009), epidemiological research has documented significant changes in both physical and psychological symptoms even among large non-clinical community samples (Hartlage et al., 2012; see also, Kiesner, 2011; Kiesner & Martin, 2013; Kiesner et al., 2016; Van Reen & Kiesner, 2016). Finally, experimental studies demonstrate that variability in response to the menstrual cycle results from individual differences in response to normal steroid changes (Schmidt et al., 1998; 2017), that may be due to genotypic differences (Huo et al., 2007; Miller et al. 2010; Smith, Sierra, Oppler, & Boettiger, 2014), and differences in genetic expression (Dubey et al., 2017). Crucially, these differences in behavioral response to cyclical hormone changes do not reflect pathological alternations of hormone *levels* (Schmidt et al., 1998) or hormone metabolism to key behavioral mediators such as neurosteroids (Nguyen et al., 2017).

This high degree of variability demonstrates that individual responses to the menstrual cycle are not homogeneous, and that *average* patterns of change across women are not likely to be meaningful. Moreover, hormone-related changes in symptoms that vary so greatly across women are not likely to *serve a similar function* for all women. Thus, theories that assume homogeneity (e.g., general group-level effects of the cycle) may fall prey to studying effects that are only relevant to a small proportion of the sample and population, and unlikely to represent the type of evolutionarily driven behavior that authors wish to study.

Methodologically, this high degree of between-person variability in response to the menstrual cycle necessitates a fundamental change in our approach to studying behavioral/symptom changes across the menstrual cycle. Simply put, because women demonstrate heterogeneous responses to the menstrual cycle, we must explicitly model these individual differences using adequate statistical methods that are designed to capture within-person covariance structures (as compared to the typical between-subjects analyses used to compare high vs. low fertility days with one-time measurement for each participant). A variety of names have been used for these essentially equivalent analyses, including hierarchical linear modeling, mixed-effects modeling, multi-level modeling, multi-level regression, and random-effects modeling. These approaches allow researchers to specifically test for, characterize, and account for individual differences across people in their response to some within-person variable, such as the menstrual cycle or steroid changes. Importantly, these analytic approaches have only recently been systematically applied to research on the menstrual cycle (Eisenlohr-Moul, DeWall, Girdler, & Segerstrom, 2015; Eisenlohr-Moul et

al., 2016; Kiesner et al., 2016; Klump et al., 2014), and have not been adopted in research testing evolutionary models of menstrual cycle-related changes in behavior. That said, it should also be recognized that these analytic strategies require repeated measures designs, which come with their own limitations and may not be well suited for some measures, such as cognitive tests that could be vulnerable to learning effects, or questions regarding values or preferences for which frequent questioning could raise suspicion and bias results.

Given the clear evidence showing large individual differences in how women respond to the menstrual cycle, we suggest that this issue be dealt with in future research. Specifically, we recommend two guidelines that will provide insights to how common the hypothesized behavior changes are across women, and possibly to what extent those variations are relevant to the evolutionary theories being tested. First, we recommend that, when possible, studies employ repeated measures designs, and adequate *multilevel* analyses that allow specific modeling of individual differences in changes across the cycle. This will provide the clearest and strongest way of quantifying the degree to which menstrual cycle-related behavior changes can be considered *universal,* or to what degree women vary in those changes. Second, when repeated measures are not possible, we recommend that researchers contextualize their work by discussing past research addressing individual differences in response to the menstrual cycle on the relevant measures. This would allow readers to consider, at least at a theoretical level, the degree to which women differ in their response to the menstrual cycle on those target behaviors. Although the second recommendation does not provide an actual solution for the problem, it does contextualize the conclusions and alert readers to the limitations of inferring that menstrual cycle-related changes are universal.

## Functional Proximal Causes vs. Third-Variable Confounds

Till now we have considered perimenstrual symptoms only in terms of being potential third-variable confounds. However, it is also possible that these perimenstrual symptoms actually have evolutionarily adaptive functions that are relevant to the theory being tested. Because this distinction is non-trivial and central to the main points presented in this paper, it is important to make this discussion as explicit and clear as possible.

Specifically, one could argue that perimenstrual symptoms are not actually third-variable confounds, but rather, are part of an evolutionarily adaptive *set* of changes that evolved specifically to drive changes in target behaviors such a mate selection and self-presentation (example behaviors studied in this evolutionary literature). In such a case, the perimenstrual symptoms discussed above could be considered as *functional proximal causes* acting between the basic physiological changes associated with the menstrual cycle, and the target social behaviors implicated in the evolutionary theory. Evolution, therefore, may have selected and shaped perimenstrual symptoms specifically, or at least partially, for the effects they exert on the target social behaviors. For example, one could hypothesize that menstrual cramps have the theoretically relevant and evolutionarily adaptive function of increasing sexual avoidance during low-fertility days (note that the same behavior change could be modeled as an *increase* in sexual interest around ovulation when cramps are absent, although this would require a different theoretical explanation). Thus, within this theoretical structure, cramps would not simply be a third-variable confound, but rather, would be a *theoretically*

*relevant and evolutionarily adaptive* variable specified within a theory of sexual avoidance (or alternatively, sexual interest). This can be contrasted with past research examining various changes in sexual interest and reproductive strategy without considering menstrual cramps, thus relinquishing them to third-variable confounds with unknown, unspecified, and untested effects or functions.

Although it is clearly possible that perimenstrual symptoms may have such theoretically-relevant evolutionarily adaptive functions, to make this argument the following two conditions must be met: (1) the perimenstrual symptoms in question must be measured and included in the analyses, and (2) those symptoms must have some plausible evolutionarily-relevant function specified within the proposed theory. For example, if menstrual cramps could potentially influence sexual interest/avoidance during days of menstruation, then a researcher must make an important decision regarding their theory and either define those effects as theoretically relevant (e.g., cramps evolved at least in part for the effects they exert on sexual avoidance during low fertility days), or define them as not theoretically relevant (e.g., cramps are simply a side effect of hypercontractility of the uterus when expelling the unused endometrial lining, and have no evolutionary-based functional role in reproductive strategy). Thus, in one case cramps are defined as a central variable in the theory, and in the other case they are treated as a potential third-variable confound. In either case, however, cramps would need to be measured and included in the statistical analyses. Because past research in this area has consistently failed to address any issues related to perimenstrual symptoms, and to our knowledge has never *argued* that perimenstrual symptoms themselves have evolutionarily adaptive functions relevant to the target theories (as functional proximal causes of target social behaviors), it is clear that neither of these two conditions have been met.

Note that, for the current discussion, what differentiates a third-variable confound from a theoretically-relevant proximal cause is whether or not the third variable is integrated into the specific theory as a theoretically-relevant proximal cause. Thus, in the hypothetical case that perimenstrual symptoms are shown to have a proximal causal role on the target behavior, if those symptoms *cannot* be integrated into the theory, then they will remain third-variable confounds that must be controlled. Moreover, the theory itself, in this case, will lack validity given that the actual proximal causes of behavior change (perimenstrual symptoms) are external to the theoretical structure. Of course, there will inevitably be cases in which our collective imagination is so limited that we will fail to see the hidden truths of nature, and thus we will occasionally overlook the actual evolutionarily functional role of some variables. Nevertheless, if any of the many changes associated with the menstrual cycle are to be conceived of as having theoretically-relevant evolutionarily adaptive functions within theories of social behaviors, then researchers must be expected to specify how these variables play such functionally adaptive roles within the specified theory, *and then* incorporate those symptoms into their empirical research. Else, they should properly recognize these symptoms as potential third-variable confounds that threaten the internal validity of their research. If, on the other hand, perimenstrual symptoms have no effects on the target behaviors, then the entire discussion of third-variable confounds becomes irrelevant.

Therefore, we propose that if authors are to hypothesize that perimenstrual symptoms have theoretically-relevant evolutionarily adaptive functions within a specified theory, rather than simply being third-variable confounds, two guidelines be followed. These recommended guidelines can easily be derived from the two conditions discussed above. First, the perimenstrual symptoms in question must be measured and included in the analyses, and second, those symptoms must be specified within the theory as potentially functional proximal causes. The extent to which these conditions are not met will proportionately degrade both the evidential and theoretical support for this potential role of perimenstrual symptoms. When neither condition is met, as in past research, there can be no support for such a theoretically relevant proximal-causal role.

### Summary

Overall, the vast number of physical and psychological changes across many tissues and systems, that are proximal to menstruation rather than ovulation, together with genetically driven individual differences in these changes, present significant methodological challenges for research on the menstrual cycle - particularly research focused on fertility. If these important sources of variance are not considered at both a theoretical and analytic level, conclusions will at best be biased, and at worst spurious. Given that research testing for evolutionarily adaptive functions for a wide variety of social behaviors has consistently failed to consider any of these issues, results and interpretations must be taken with great caution, as these failures in scientific rigor will lead to conclusions that lack internal validity, and lead to misguided theoretical inference.

## Conceptual Issues

In the present section we discuss two conceptual issues that should be addressed in research attributing an evolutionarily adaptive function to behaviors that fluctuate across the menstrual cycle. First, we address the *need to specify more sophisticated theories* that consider the complexity of biological, physical, psychological, and social changes that occur across the menstrual cycle; and second, we address the need to *more carefully select target phenotypes that may actually have an evolutionarily adaptive function*. In addition to outlining these issues and their importance in this area of research, we will also propose specific guidelines for addressing them in research.

### Need to Specify Biological, Psychological, and Social Pathways

In a recent theoretical paper, Kiesner (2017) suggested that physical and psychological changes directly associated with the menstrual cycle could have broader implications for long-term social and affective development. Specifically, it was argued that the many changes of the menstrual cycle, affecting various tissues throughout the body (e.g., gastrointestinal, skin, immune, CNS, liver, breast), could interfere with successful engagement in important developmental tasks such as school, social, and sports activities. This, in turn, could lead to negative changes in relatively stable aspects of psychological and behavioral adjustment, such as chronic disengagement, attributional style, body-image dissatisfaction, and depression.

This theoretical framework is important for the present discussion because it emphasizes the need to consider and specify all levels of biological, physical, psychological and social influences in the pathways leading from the menstrual cycle to behavioral and psychological outcomes. For example, the causal pathway from the menstrual cycle to changes in *body-image dissatisfaction* could be hypothesized to start with direct effects of reproductive steroids on diverse CNS tissues (for discussion on neural plasticity in relation to reproductive steroid fluctuations, see, McEwen, Akama, Spencer-Segal, Milner, & Waters, 2012; Ossewaarde et al., 2013), that may result in behavioral and affective changes associated with the menstrual cycle such as food cravings, feeling out of control, anxiety, irritability, and depression (Freeman et al., 1996; Steiner et al., 2011). These psychological changes could then influence behaviors such as impulsive and emotional eating (Klump et al., 2013, 2014), which could be reinforced and maintained by their ameliorating effects on negative affect, through direct gut-to-brain signaling (see for example, Van Oudenhove et al., 2011, who suggest that direct gut-to-brain signaling through activation of vagal nerve afferents are likely to account for the attenuation of negative affect following intragastric infusion of fatty acid solution). These changes in eating, combined with premenstrual fluid retention (Freeman et al., 1996; Rosenfeld et al., 2008), weight gain, and abdominal heaviness/discomfort (Rosenfeld et al., 2008), as well an increase in acne (Arora, Seth, & Dayal, 2010; Kiesner & Pastore, 2010), may result in increased levels of body-image dissatisfaction, which has been repeatedly found to peak perimenstrually (Carr-Nangle et al., 1994; Jappe & Gardner, 2009), and which could further change social and health behaviors. Thus, in this framework, multiple levels and pathways considering a wide range of menstrual cycle-related symptoms are recognized for their potential roles in the outcome, which itself may have feedback loops acting on *upstream* variables, such as those named above.

Note that this approach to studying the menstrual cycle takes the emphasis off of specific steroid effects and emphasizes the need to consider the menstrual cycle as an integrated and complex set of changes across multiple levels and domains of the individual's life. Moreover, within this context, when one refers to "pathways" of effects, one is referring to pathways involving biological changes, behavioral changes, psychological changes, and social changes. Thus, without considering the complexity of changes across these levels, and within a developmental context, theories and conclusions will be exceedingly simplistic and inadequate for understanding the behavioral phenotypes under examination. Rather, providing a thorough analysis of all potential pathways, and how they can be integrated within an evolutionary perspective, should be considered an essential part of theory development and research in this area. Simply demonstrating a temporal link between the menstrual cycle and some target behavior does not represent an adequately sophisticated approach, or an adequate test of a theory.

Therefore, as a guideline for menstrual cycle-related evolutionary theory and research, we suggest that careful assessments be explicitly presented considering the many biological, physical, psychological, and social changes associated with the menstrual cycle, providing rationale and insights on how these variables may influence the target behavior. Moreover, it is essential that these efforts go beyond simple main-effects questions such as "Can menstrual cycle-related acne, or cramps, or mood swings, influence some target behavior?"

Rather, it is important to consider the possibility that multiple levels of change (biological, physical, psychological, social) may work together to produce changes in more distal complex social behaviors. For example, as described above, changes in body-image dissatisfaction may be influenced by a broad set of changes such as appetite, emotional eating, emotional regulation, water retention, and acne, that may mutually influence each other as well as body-image dissatisfaction (which itself may influence a broad range of other variables), all of which may influence target social behaviors such as mate selection and self-presentation. Clearly, this approach is burdensome and requires a sophisticated understanding of the menstrual cycle as an integrated and complex set of changes, yet the alternative, as with any field of inquiry, is that years of research are later dismissed for their theoretical weakness and lack of internal validity.

## Not all Phenotypes are Functionally Adaptive or Relevant

Gould and Lewontin (1979) roundly criticized what they referred to as the "adaptationist programme" within evolutionary theory, in which organisms are viewed as collections of discrete characteristics or traits that have each evolved independently through natural selection, thus ignoring the wholeness of the organism as an integrated entity. Although this criticism was written nearly 40 years ago, and not focused on the possible adaptive functions of menstrual cycle-related phenotypes, their points are relevant to the body of research addressed in the present paper. Specifically, across studies addressing many heterogenous behavioral phenotypes, this body of research habitually takes each single phenotype as a discrete *atomized* unit to be analysed. In doing so, these behavioral phenotypes are studied in isolation from the many other changes associated with the menstrual cycle. Moreover, Gould and Lewontin also emphasized the failure of the adaptationist programme "to distinguish current utility from reasons of origin", or as we will more broadly address this issue – failure to distinguish reasons of origin from *any* functional utility.

Before entering the arguments specific to the menstrual cycle, it is important to note that just because a *genotype has an evolutionarily adaptive function* does not suggest that all associated phenotypes are functionally adaptive. Although this may seem paradoxical, a simple example, unrelated to the menstrual cycle, will clarify the point. Most cases of sickle-cell anaemia (≈70%; see Williams & Obaro, 2011) are the result of having two copies (homozygosity) of a mutated beta-globin gene, affecting the haemoglobin protein in red blood cells, and resulting in this debilitating and potentially fatal genetic illness (Aidoo et al., 2002; Williams & Obaro, 2011). Although such a mutation would seem maladaptive, heterozygosity for the mutation has the evolutionary benefit of protecting against malaria without resulting in sickle cell disease (Aidoo et al., 2002; Williams & Obaro, 2011), and is also more common than homozygosity. Thus, although both homozygosity and heterozygosity confer malarial protection, the cost of homozygosity outweighs the benefits, and is thus not adaptive. Therefore, the actual phenotype of sickle cell anaemia is the product of an evolutionarily adaptive mutation (when heterozygous), even though homozygosity and the disease itself are not functionally adaptive.

With the menstrual cycle, there are several corollaries of phenotypes that are unlikely to have functional roles, but may be the products of other biological changes that do have

functional roles. Menstrual cycle-related acne, for example, is likely the consequence of endophenotypes such as menstrual cycle regulation of immune function (Bertone-Johnson et al., 2014; Blum et al., 2005; Puder et al., 2006), and serum lipid profiles (e.g., triglycerides and cholesterol; Arora et al., 2010). In relation to immunity, the link between steroid changes and inflammation has likely evolved, in part, to protect a developing fetus from an immune response of the mother (Robinson & Klein, 2012). Thus, while the genetics that regulate menstrual cycle changes in immune function and serum lipid profiles may be adaptive and important for other biological functions, cyclical changes in acne itself probably has no evolutionarily adaptive function. Another example regards menstrual cramps, which result from hypercontractility of the uterus (Dawood & Khan-Dawood, 2007) and are part of a natural and necessary process of expelling the unused endometrial lining. Thus, such cramps can be considered to be a negative side effect of a necessary biological process, and there should be no need to associate these cramps with an evolutionarily adaptive reproductive strategy, such as sexual avoidance during low-fertility days. Similar contractile pain of the uterus occurs at child birth, and we would scarcely argue that those pains have evolved to prevent sexual contact during child birth. Thus, there are likely many changes associated with the menstrual cycle which have no evolutionarily adaptive function (including social behaviors), but are simply side-effects of other changes (observable or not).

These examples involving physical symptoms of the menstrual cycle may seem exceedingly distant from the social behaviors studied in the context of evolutionary theory. However, past research has shown that physical and psychological symptoms of the menstrual cycle are robustly associated with each other (e.g., women who have more physical menstrual symptoms also have more psychological symptoms; Kiesner, 2009; Kiesner et al., 2016). This association suggests that physical and psychological symptoms either share a common causal factor (e.g., steroid sensitivity), and/or that one causes the other, for example that physical symptoms lead to psychological symptoms (previously referred to as the *physical distress hypothesis*, Kiesner & Pastore, 2010). Psychological symptoms of the menstrual cycle may also result from cyclical changes in inflammatory cytokine signaling by the immune system (see Blum et al., 2005, and Puder et al., 2006, for evidence of menstrual cycle-related changes in inflammation, and menstrual cycle-linked covariation of inflammation and affective symptoms, respectively), with over 30 years of research linking inflammatory signaling with a variety of behavioral and mood changes (e.g., “sickness behavior”; Dantzer & Kelley 2007). Thus, changes in psychological symptoms may partly be epiphenomena of the many other physiological and physical changes of the cycle, which are themselves endophenotypes of more basic biological processes, many of which likely evolved to support pregnancy rather than conception.

Finally, if we are compelled to postulate that PMS symptoms, or other behavioral changes of the menstrual cycle, are part of an adaptive phenotypic response to the menstrual cycle, what shall we argue regarding the vast array of other behavioral phenotypes associated with the menstrual cycle, including suicide (MacKinnon & MacKinnon, 1956; Saunders & Hawton, 2006), accidental deaths (MacKinnon & MacKinnon, 1956), emotional eating (Klump, Keel, Culbert, & Edler, 2008; Racine et al., 2013), tobacco use (Marks, Hair, Klock, Ginsburg, & Pomerleau, 1994; Sakai & Ohashi, 2013), alcohol use (Kiesner, 2012; Marks et al., 1994; Martel, Eisenlohr-Moul & Roberts, 2017), and the subjectively experienced effects of

amphetamines and cocaine (see, Terner & de Wit, 2006)? Similarly, what can be inferred about menstrual cycle-related changes in hospital admission rates for psychiatric illness (Dalton, 1959)? Following the trend in evolutionary research, we could be expected to attribute evolutionarily adaptive functions to psychotic hallucinations and suicide attempts during menstruation (presumably related to changes in reproductive strategy). We doubt that there are such adaptive functions, either presently or in past evolutionary epochs. Moreover, because hypotheses attributing evolutionary function to these phenotypes can never be adequately tested, and because there are many alternative mechanisms and alternative hypotheses for explaining menstrual cycle-related changes in these behaviors, we must exercise caution in selecting which behaviors/phenotypes we attempt to attribute to some evolutionarily adaptive function.

Given the above discussion, and the specific examples we've provided, it should be clear that more attention needs to be given to selecting target behaviors that may actually have evolutionarily adaptive functions. Although this will be an abstruse task, with a low level of certainty, an important first step will be to consider how the *presence* and *possible functions* of menstrual cycle-related symptoms may influence target behaviors. For example, by considering the *actual cause* of menstrual cramps (hypercontractility of the uterus when expelling the endometrial lining), it becomes clear that any evolutionary theory linking reproductive strategy with social behavior changes that may actually be driven by cramps, would be an egregiously weak theory, unless the cramps themselves were integrated as a theoretically relevant proximal cause. Specifically, if the proximal causes of an outcome are external to the theory, then the theory itself is weak or indefensible. Thus, as a guideline, we recommend that authors provide a rationale for why the target phenotype is better explained by the proposed theory than by some third-variable confounds related to the wide range of changes associated with the menstrual cycle; or alternatively, how those menstrual cycle-related symptoms could act in a theoretically meaningful way as functional proximal causes.

This guideline requires the consideration of a broad set of physical and psychological changes associated with the menstrual cycle, and an evaluation of whether they may function as evolutionarily-relevant proximal causes, or simply as third-variable confounds. This approach is very similar to what is used in developmental studies which often depend on correlational designs that require an exhaustive assessment and statistical control of many variables that may not be integral to the theory itself, but are essential for establishing a study's internal validity. Although challenging, taking these steps will help researchers consider the entirety of the human menstrual cycle as an integrated and complex set of changes, make theoretically more defensible selections of target behaviors, and avoid the traps of the "adaptationist programme" discussed by Gould and Lewontin (1979).

## Summary

We have discussed two important conceptual issues that have not been adequately addressed in research attributing menstrual cycle-related behavioral changes to hypothesized evolutionarily-adaptive functions. The lack of attention to these conceptual issues suggests that this area of research may be addressing behaviors that, although correlated with the menstrual cycle, have no functionally adaptive role that is specific to the menstrual cycle or

the theory being tested. In the absence of more sophisticated models that acknowledge individual differences in the vast array of interconnected physiological, physical, social, and psychological changes associated with the menstrual cycle, explicit justification for the selection of target phenotypes, and more robust controls for confounds, continued use of the ovulation-focused evolutionary framework is misguided.

## Discussion

In the present paper we have argued that recent empirical work attributing menstrual cycle-related changes in non-reproductive behaviors to evolutionarily adaptive functions has suffered from methodological and conceptual weaknesses, and therefore, these studies do not provide support for the proposed theories. As a result, conclusions have been promoted that are not scientifically justified, leading to significant theoretical overreach.

One central limitation is that studies in this area consistently fail to consider the complexity of the menstrual cycle and the many changes that occur during the cycle, across the entire body, that could easily influence the outcome variables studied. This omission creates a significant third-variable confound within these studies. Simply put, because the menstrual cycle is associated with many biological changes across the body that may influence a wide variety of both physical and psychological variables, there remain many unanswered questions about cause-effect relations, as well as adaptive functions, of these variables. For example, if some target behavior changes across the menstrual cycle because of cyclical changes in headaches, then an inferred evolutionary function of the behavior itself, without considering the cause and *function* of the headaches, is dubious at best. Thus, without considering these confounds, the results and conclusions cannot be interpreted with confidence. As noted throughout the current paper, this omission is surprising given its obvious potential and the meaningful changes in theoretical interpretation.

Related to this first limitation, we have primarily advocated addressing these issues in two ways. First, we have argued that if any perimenstrual symptoms can be defined as theoretically-relevant proximal causal variables within the theory being tested, rather than simply third variable confounds, it is paramount that they be incorporated into better defined and more complete theoretical models. Second, regardless of whether or not they are theoretically-relevant proximal causes within the specific theory, it is paramount to measure and analytically control for these potential confounds. Although the first point should be considered essential for any sophisticated test of theory, the second point could potentially be addressed by experimentally manipulating levels of steroid hormones, rather than statistically controlling for the perimenstrual symptoms themselves. Although technically possible, practical and ethical concerns regarding pharmacological manipulations of steroids, especially when there would be no expected clinical benefit, significantly limits its use in this area of research.

That said, there are other experimental or quasi-experimental approaches that could provide indirect evidence regarding the causal role of perimenstrual symptoms in the target behaviors studied in this area of research. For example, feelings of physical discomfort or pain, or perceptual changes related to body image (e.g., water retention, oily skin), could be

manipulated experimentally as analogues of similar perimenstrual symptoms. Although the actual symptoms associated with the menstrual cycle are far more complicated than those that could be created in a lab (e.g., history of monthly recurrence, combination of multiple symptoms, extended duration of symptoms across days rather than just minutes or hours), the presence of effects on relevant target behaviors would provide compelling evidence that similar symptoms could influence behavior across the menstrual cycle (null effects on the other hand would not provide compelling evidence for the absence of such effects). Alternatively, one could test for changes in social behavior that are related to feeling sick from a cold or flu, from a night of heavy drinking, or following an injury. In each of these cases one could hypothesize that distressing or painful symptoms would predict behavior changes similar to those observed when perimenstrual symptoms are highest, independent of the menstrual cycle or fertility. Finally, including male control groups who experience similar symptoms (e.g., recurrent headaches, joint pains, depression, anxiety, acne flareups) that could precipitate similar changes in relevant target behavior (mate attraction, sexual interest, self-presentation, tips earned when performing lap dances) may provide a quasi-experimental approach to testing whether similar symptoms result in similar behavior changes, even when there could be no plausible explanation linked with the evolutionary functions of the menstrual cycle, or fertility *per se*.

A second important issue is that *proximity to ovulation*, which is a key theoretical construct across these studies, is simply the inverse of *proximity to menstruation*. As a result, any effects found for *proximity to ovulation* may just as easily be explained in terms of *proximity to menstruation*. This is a non-trivial issue because conclusions and theoretical inference in this evolutionary literature depend on behavioral changes being driven by ovulation, rather than menstruation. Nonetheless, this issue has not been addressed in this literature, underlining a lack of attention to what the menstrual cycle involves and how the wide range of menstrual cycle changes may influence human behavior. This omission is somewhat surprising, given the copious literature on the perimenstruum and associated physical and behavioral correlates.

A third concern regards the failure, across studies, to test for individual differences. By ignoring individual differences these theories and studies presume a homogeneous response to the menstrual cycle across women. However, because a broad base of evidence shows that women do not respond to the menstrual cycle in a homogeneous way, it is very possible that the observed effects are driven by a small proportion of women. Comparison with PMS illustrates the importance of this issue. For decades, many had assumed that PMS symptoms were the norm, yet, although research has shown that large community-based samples of women do experience some level of PMS symptoms (e.g., Hartlage et al., 2012), only about 6–8% experience clinically severe levels of these symptoms (Angst, Sellaro, Stolar, Merikangas, & Endicott, 2001; Cohen et al., 2002; Gehlert et al., 2009). Moreover, research has also shown that some women even feel better perimenstrually (Kiesner, 2011). This high level of heterogeneity is important not only at a methodological level, but also at a theoretical level, because it requires theorists to carefully consider, and verify, that the behaviors they are studying are in fact normal, and affect most or all women in a similar way. If the behaviors studied affect only a minority of women, then the authors would need to specify how that fits in with an evolution-based theory.

We have also argued that in many cases it is unnecessary to invoke evolutionary theory to explain observed phenotypes, as those phenotypes are likely to be the indirect and non-functional outcome of some other adaptive change(s) also associated with the menstrual cycle. Simply, not all phenotypes have an evolutionarily adaptive function, and therefore do not require an evolutionary theory to explain such a function. Careful examination of evolutionary research on the menstrual cycle can leave one with the impression that a temporal correlation with ovulation (or the menstrual cycle in general) is considered sufficient cause to argue for an evolutionarily adaptive function. We, however, do not believe that a mere temporal correlation is adequate evidence for the theoretical inferences that are often made.

The combination of these limitations suggests that target variables and their putative evolutionarily adaptive functions must be integrated into more comprehensive causal models which consider the full range and variability of menstrual cycle-related changes in biological, psychological, and social processes. For example, if menstrual cycle-related changes in a specific social behavior are also correlated with menstrual cramps and water retention (e.g. both within person and across persons), which may in turn affect mood, behavioral engagement, body-image dissatisfaction, and social relationships, then the causal model must fully integrate this diverse set of changes, and consider possible causal links among them. Thus, we argue that pursuing evolutionary models - without explicitly considering these many complex changes - will lead to spurious support for weak and underdeveloped theoretical structures.

It should again be emphasized that our objections are not with evolutionary theory *per se*. There should be no doubt that most biological aspects of the menstrual cycle have evolved for some important function, and that relevant psychological and behavioral changes will in some way depend on those biological changes (including changes in CNS function). Our concerns, rather, lie with the lack of attention to possible third variables and individual differences across women, the likelihood that observed changes rely on proximity to menstruation, rather than ovulation, and reliance on overly simplistic theoretical models that fail to consider these issues in a comprehensive way.

Overall, our conclusions are that theorists studying the menstrual cycle - whether from an evolutionary or non-evolutionary framework - must apply *(1)* more rigorous criteria for selecting specific phenotypes to be studied, *(2)* more rigorous methods, including statistical control of other changes associated with the menstrual cycle, *(3)* more careful consideration of proximity to menstruation vs. proximity to ovulation, *(4)* must consider the possibility that some phenotypes are driven by an abnormal response to steroids, and do not actually represent the norm, and *(5)* must develop more sophisticated and comprehensive theoretical structures consonant with the complexity of the menstrual cycle. Note that these issues are not separate and distinct. For example, a good theoretical structure should already consider all possible third-variable confounds, which in this case will include the many changes and symptoms of the menstrual cycle, as well as the issue of proximity to menstruation. Although we cannot infer that researchers in this area have not considered these issues, they are consistently not formally addressed. Because they represent obvious and important confounds that threaten the internal validity of research in this area, we argue that these

issues must be explicitly and formally addressed at all levels, including theory development, research design, and data analysis.

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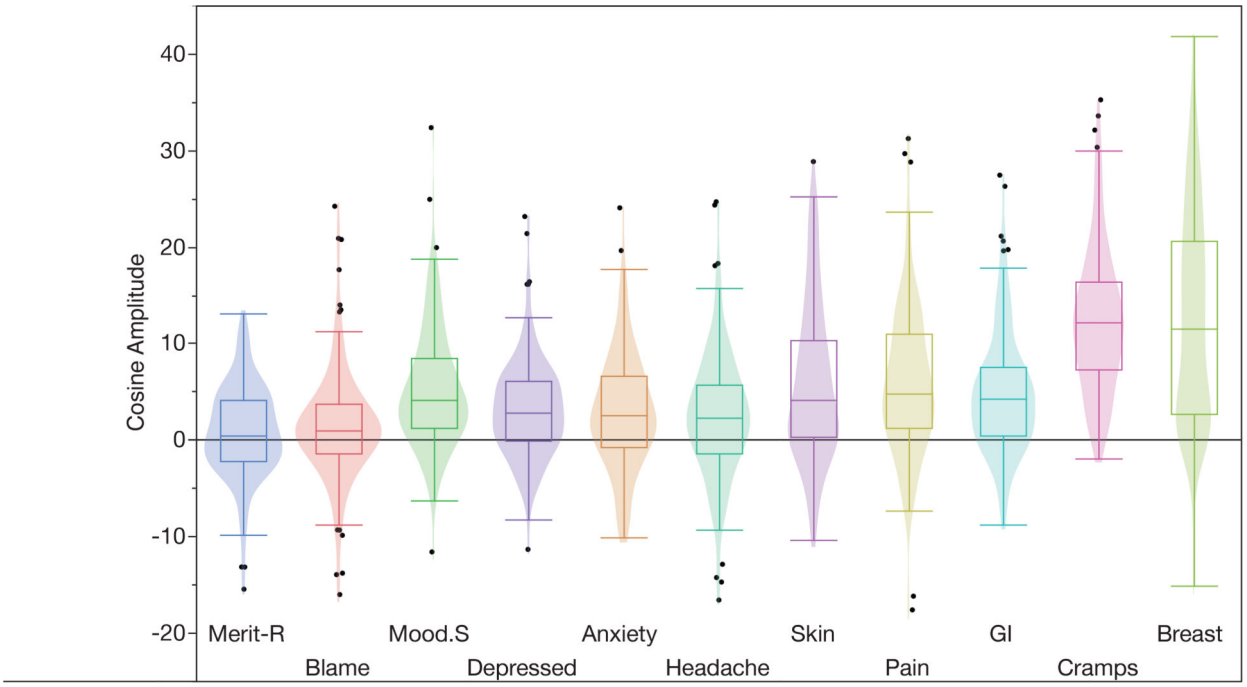
## Statement of Public Significance

Research attributing evolutionarily adaptive functions to menstrual cycle-related changes in psychological and behavioral variables has overlooked key aspects of the menstrual cycle that could explain study results. More sophisticated theories and methods will be required to fully test the evolutionary hypotheses proposed in the literature. Recommended guidelines are presented.




| | Merit-R | Blame | Mood.S | Depressed | Anxiety | Headache | Skin | Pain | GI | Cramps | Breast |
|---|---|---|---|---|---|---|---|---|---|---|---|
| % Var Fixed | 0.1 | 0.2 | 3.4 | 1.6 | 1.0 | 1.0 | 4.3 | 3.8 | 2.9 | 14.4 | 18.1 |
| % Var Random | 1.5 | 2.2 | 6.6 | 4.0 | 3.8 | 3.1 | 11.3 | 8.4 | 6.4 | 18.3 | 30.7 |

**Figure 1:**

Box plots, contour plots, and effect sizes of cosine amplitude coefficients (measure of direction and magnitude of cyclical change) for a variety of psychological and physical symptoms. Note: “% Var Fixed” is the proportion of within-person variance accounted for by the average effect of the cosine function across individuals; and “% Var Random” is the proportion of within-person variance accounted for by individual differences in the cosine function. Used with permission: Kiesner, J., Mendle, J., Eisenlohr-Moul, T. A., & Pastore, M. (2016). Cyclical symptom change across the menstrual cycle: Attributional, affective, and physical symptoms. Clinical Psychological Science, 4(5), 882–894.

**Table 1.**

Common Menstrual Cycle-Related Experiences and Possible Behavioral/Psychological Confounds

| Experience | Physiology | Behavioral and Psychological Covariates/Confounds |
|---|---|---|
| Headaches/Migraines | Neurovascular disturbance [1]; neurogenic inflammation [2]; sensitization of trigeminal system [3]. | Depressed mood; irritability; changes in support seeking; decreased physical activity; social withdrawal; decreased sexual interest. |
| Lower Abdominal Cramps | Prostaglandin induced uterine hypercontractility [4, 5]. | Immobility due to pain; decreased physical activity; social withdrawal; irritability; decreased sexual interest. |
| Bloating:<br>Weight gain<br>Breast pain | Water retention [6]. | Changes in dress to accommodate physical shape changes; decreased physical activity; social withdrawal; lower self-esteem; body image dissatisfaction. |
| Acne | Changes in lipids [7, 8], sebum, hydration, and collagen production [8]; immune regulation. [8, 9, 10] | Lower self-esteem; social withdrawal; body image dissatisfaction. |
| GI Changes | Immune regulation [8, 9, 10]; nutrient absorption [11]; gastric motility/ transit [12]. | Decreased physical activity; decreased energy; decreased sexual interest. |
| Mood Changes (PMS/PMDD) | Serotonin involvement [13, 14]. GABA receptor involvement [15, 16]. | Decreased physical activity; social withdrawal; social conflict; changes in support seeking; decreased sexual interest. |

[1] Goadsby, Lipton, & Ferrari, (2002)

[2] Waeber & Moskowitz, (2005)

[3] Martin (2008)

[4] Dawood, (2006)

[5] Dawood, & Khan-Dawood, (2007)

[6] Chapman et al., 1997

[7] Arora, Seth, & Dayal, (2010)

[8] Farage, Neill, & MacLean, (2009)

[9] Bertone-Johnson et al., (2014)

[10] Puder et al., (2006)

[11] Xu et al., (2003)

[12] Liu, Chen, Liu, Xie, & Wang, (2002)

[13] Rubinow, Schmidt, & Roca, (1998)

[14] Freeman, Frye, Rickels, Martin, & Smith, (2002)

[15] Andréen et al., (2009)

[16] Epperson et al., (2002).