Adaptive Human Behavior and Physiology
https://doi.org/10.1007/s40750-022-00208-5

ORIGINAL ARTICLE

Is Pathogen Disgust Increased on Days of the Menstrual Cycle when Progesterone is High? Evidence from a Between-Subjects Study Using Estimated Progesterone Levels

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Received: 23 September 2022 / Revised: 16 December 2022 / Accepted: 19 December 2022

Abstract

Objective The Compensatory Prophylaxis Hypothesis proposes that women will show increased pathogen disgust at points in the menstrual cycle when progesterone is high, compensating for the immunosuppressive effects of progesterone. However, evidence for the Compensatory Prophylaxis Hypothesis from studies that used longitudinal designs to investigate whether pathogen disgust tracks changes in progesterone is mixed. It was recently proposed that longitudinal designs may be poorly suited to testing the Compensatory Prophylaxis Hypothesis because carry-over effects when women are tested repeatedly in within-subject designs might obscure the effects of progesterone and pathogen disgust. Consequently, we used a between-subjects design to test for a positive relationship between scores on the pathogen disgust subscale of the Three Domain Disgust Scale and progesterone levels imputed from menstrual cycle data using actuarial tables.

Methods We employed a between-subject design on $N=1346$ women using the Three Domains of Disgust Scale (TDDS).

Results We found no evidence for a positive effect of progesterone on pathogen disgust, suggesting that null results for the hypothesized relationship between progesterone and pathogen disgust are not limited to studies using designs that may be subject to carry-over effects caused by repeated testing.

Conclusion Our results add to a growing body of research that does not support the Compensatory Prophylaxis Hypothesis.

Keywords Compensatory Prophylaxis Hypothesis · Pathogen disgust · Progesterone · Menstrual cycle

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Published online: 27 December 2022

Introduction

Suppressed physiological immune responses during the luteal phase of the menstrual cycle (when raised progesterone prepares the body for pregnancy) reduce the likelihood that the physiological immune system will undermine the development of the blastocyst (reviewed in Fleischman & Fessler, 2011). The Compensatory Prophylaxis Hypothesis suggests that this luteal-phase immunosuppression is associated with increased disgust toward pathogen cues that compensates for the reduction in physiological immune responses by reducing the probability of contact with pathogens (Fessler et al., 2005; Fleischman & Fessler, 2011). Three recent studies have directly tested the Compensatory Prophylaxis Hypothesis by investigating how pathogen disgust changes as a function of progesterone levels and/or menstrual cycle phase using longitudinal designs. However, these studies have reported mixed evidence for the Compensatory Prophylaxis Hypothesis.

Jones et al. (2018) tested whether 357 women's scores on the pathogen disgust subscale of the Three Domain Disgust Scale (Tybur et al., 2009) increased on days of the menstrual cycle where progesterone was high, finding no evidence that pathogen disgust tracked changes in progesterone. However, progesterone was measured from saliva samples via immunoassays, which is a method that has recently been criticized for having relatively modest validity when measuring changes in progesterone levels during the menstrual cycle (Arslan et al., 2022). To address this potential limitation, Stern and Shiramizu (2022) tested whether 257 women's scores on the pathogen disgust subscale of the Three Domain Disgust Scale and scores on the contamination subscale of the Revised Padua Obsessive-Compulsive Inventory (Burns et al., 1996) increased on days of the menstrual cycle where progesterone was high when liquid chromatography-mass spectrometry was used to measure progesterone level from saliva. Using this method, Stern and Shiramizu (2022) found no evidence that pathogen disgust tracked changes in progesterone and also found no evidence for increased pathogen disgust during the luteal phase of the menstrual cycle. By contrast with the null results reported by Jones et al. (2018) and Stern and Shiramizu (2022), Miłkowska et al. (2021) reported that pathogen disgust (assessed using the pathogen disgust subscale of the Three Domain Disgust Scale, the contamination subscale of the Revised Padua Obsessive-Compulsive Inventory, and disgust ratings of images depicting pathogen cues) increased significantly during the luteal phase of the menstrual cycle in a sample of 93 women. Note that Miłkowska et al's (2021) study did not measure progesterone levels.

Given (1) the mixed evidence for the Compensatory Prophylaxis Hypothesis reported in the longitudinal studies described above and (2) the recent suggestion that carry-over effects when pathogen disgust is assessed repeatedly in longitudinal studies might obscure progesterone-linked changes in pathogen disgust (Bressan & Kramer, 2022), the current study used a between-subjects design to test for a positive relationship between scores on the pathogen disgust subscale of Tybur et al's (2009) Three Domain Disgust Scale and progesterone levels imputed from menstrual cycle data using a method described in Arslan et al. (2022).

Table 1 Descriptive statistics for the Three Domain Disgust Scale

Disgust Subscale	Mean	Standard Deviation	Cronbach's alpha
pathogen disgust	3.77	1.07	0.74
sexual disgust	2.86	1.29	0.79
moral disgust	3.85	1.31	0.88

Methods

Data Collection

Participants in this online study were *N=1346* women (Mean $_{Age}$ = 24.25 years, SD $_{Age}$ = 7.2 years, range $_{Age}$ = 16 to 52 years), none of whom reported being pregnant or having given birth in the last year. None reported currently using any form of hormonal contraception or hormone replacement therapy. Additionally, none of the women reported having stopped using any form of hormonal contraception in the last three months or reported having stopped menstruating for any reason (e.g., menopause). Each woman reported the date of the onset of their most recent (i.e., last) menses and the expected date of the onset of their next menses. The study was advertised via a number of social media platforms (e.g., stumbleupon.com). Participants took part on a voluntary basis and were recruited between July 2008 and February 2016.

Each woman also completed Tybur et al.'s (2009) Three Domain Disgust Scale, which asks participants to rate each of 21 actions from not at all disgusting (0) to extremely disgusting (6). The Three Domain Disgust Scale divides actions into three domains: pathogen disgust (e.g., stepping on dog poop), sexual disgust (e.g., 3 hearing two strangers having sex), and moral disgust (e.g., deceiving a friend). Responses are then averaged to produce a score for each of the three domains, with higher scores indicating greater disgust. Descriptive statistics are shown in Table 1. Data were collected using the Experimentum platform (DeBruine et al., 2020).

Initial Processing of Data

For each woman, the date of their last menses and the date for their next menses were used to calculate cycle day using both the backward-counting method and the forward-counting method. Cycle-day data were then used to impute progesterone and estradiol levels using an algorithm described in (and developed by) Arslan et al. (2022). These values were imputed separately for the forward-counting and backward-counting methods. Arslan et al. (2022) have previously demonstrated that estradiol and progesterone values imputed in this way using the forward- and backward-counting methods are highly correlated with values measured from serum (progesterone: r=0.83 or 0.87, respectively; estradiol: r=0.68 or 0.72, respectively). By contrast, Arslan et al. (2022) reported that correlations between values from salivary immunoassays and from serum were substantially weaker. Arslan et al's algorithm can only impute progesterone and estradiol values for cycle days between days −1 and −40 when the backward-counting method is used and days 1 and 39 when the forward-counting method is used and imputes log-transformed values. In our sample of 1346 women, progesterone and estradiol levels could be imputed for 1304 women

Table 2 Results of regression analyses when pathogen disgust was the outcome variable

	Estimates (std. Beta)	SE (standardized)	t	P	95% CI
Model with backward-counting method (*N* = *1313*)					
Progesterone	0.06	0.05	1.20	0.229	-0.03–0.15
Estradiol	0.00	0.04	0.03	0.980	-0.08–0.09
Progesterone x Estradiol	-0.01	0.05	-0.27	0.786	-0.11–0.08
Age	-0.03	0.03	-0.93	0.354	-0.08–0.03
Model with forward-counting method (*N* = *1304*)					
Progesterone	0.04	0.03	1.28	0.200	-0.02–0.10
Estradiol	-0.04	0.03	-1.10	0.271	-0.10–0.03
Progesterone x Estradiol	-0.02	0.04	-0.49	0.624	-0.10–0.06
Age	-0.03	0.03	-1.15	0.251	-0.09–0.02

using the forward-counting method and 1313 women using the backward-counting method (i.e., hormone levels could not be imputed in a small number of cases where the cycle day was outside the range for which Arslan et al. provide estimates).

Results

Raw data, analysis code, and full outputs are publicly available on the Open Science Framework (https://osf.io/9fqcm/). Analyses were conducted using R statistical software version 4.2.0, RStudio version 2022.2.2.485, and the packages dplyr 1.0.9 (Wickham et al., 2022), tidyverse 1.3.1 (Wickham, 2022), kableExtra 1.3.4 (Zhu, 2021), psych 2.2.5 (Revelle, 2022), lubridate 1.8.0 (Spinu, Grolemund, and Whickman, 2021), jtools 2.2.0 (Long, 2022), sjPlot 2.8.10 (Lüdecke, 2021).

We used linear regression analyses to test for possible relationships between scores on the three subscales of the Three Doman Disgust Scale and estimated hormone levels. Each combination of disgust subscale (i.e., pathogen, sexual, or moral disgust) and method used to impute hormone levels (i.e., forward-counting or backward-counting method) were analyzed in separate models. In each model, disgust score was the outcome variable and estimated progesterone, estimated estradiol, their interaction, and participant age were predictors. All predictors were converted to z-scores prior to analyses. We included age as a covariate in light of previous research reporting age-related declines in pathogen disgust (e.g., Curtis et al., 2004). Model diagnostics (DFbetas and distribution of residuals) did not indicate any influential cases or deviation from the assumption of normality and homogeneity of residuals (see Field et al., 2012).

Pathogen Disgust

For pathogen disgust, neither model showed any significant relationships. Results of these analyses are summarized in Table 2.

Table 3 Results of regression analyses when sexual disgust was the outcome variable

	Estimates (std. Beta)	SE (standardized)	t	P	95% CI
Model with backward-counting method (*N* = *1313*)					
Progesterone	0.02	0.05	0.54	0.592	-0.07–0.11
Estradiol	-0.02	0.04	-0.53	0.599	-0.11–0.06
Progesterone x Estradiol	-0.05	0.05	-1.04	0.297	-0.14–0.04
Age	-0.14	0.03	-5.29	< **0.001**	-0.20 – -0.09
Model with forward-counting method (*N* = *1304*)					
Progesterone	0.00	0.03	0.08	0.937	-0.06–0.06
Estradiol	0.01	0.03	0.44	0.659	-0.05–0.08
Progesterone x Estradiol	-0.02	0.04	-0.38	0.705	-0.10–0.07
Age	-0.14	0.03	-4.96	< **0.001**	-0.19 – -0.08

Table 4 Results of regression analyses when moral disgust was the outcome variable

	Estimates (std. Beta)	SE (standardized)	t	P	95% CI
Model with backward-counting method (*N* = *1313*)					
Progesterone	-0.01	0.05	-0.27	0.788	-0.10–0.08
Estradiol	0.02	0.04	0.58	0.565	-0.06–0.11
Progesterone x Estradiol	0.01	0.05	0.16	0.877	-0.09–0.10
Age	0.17	0.03	6.27	< **0.001**	0.12–0.22
Model with forward-counting method (*N* = *1304*)					
Progesterone	0.04	0.03	1.25	0.211	-0.02–0.10
Estradiol	-0.00	0.03	-0.02	0.983	-0.07–0.06
Progesterone x Estradiol	-0.03	0.04	-0.75	0.451	-0.11–0.05
Age	0.17	0.03	6.17	< **0.001**	0.12–0.22

Sexual Disgust

For sexual disgust, neither model showed any significant relationships for the hormone-level predictors, but both models showed significant negative relationships between participant age and sexual disgust. Results of these analyses are summarized in Table 3.

Moral Disgust

For moral disgust, neither model showed any significant relationships for the hormone-level predictors, but both models showed significant positive relationships between participant age and sexual disgust. Results of these analyses are summarized in Table 4.

Repeating the analyses described above, this time with progesterone as the only predictor or with only progesterone and participant age as predictors, showed the same patterns of results (i.e., did not reveal any significant relationships between progesterone and disgust, see https://osf.io/9fqcm/ for full results of these analyses).

Table 5 Results of correlation between estimated progesterone and pathogen disgust

	r	df	t	P	95% CI
Backward-counting method (N = 1313)	0.05	1311	1.90	0.057	0.00–0.11
Forward-counting method (N = 1304)	0.02	1302	0.90	0.368	-0.03–0.08

Robustness Checks

We carried out further analyses (i.e., robustness checks) in which we repeated all of the analyses described above, this time including only (1) women for whom the number of days reported between the onsets of their last and next menses were between 20 and 35 days (1131 women met this criterion using the forward-counting method and 1131 women met this criterion using the backward- counting method) and (2) women for whom the number of days reported between the onsets of their last and next menses were between 25 and 35 days (1075 women met this criterion using the forward-counting method and 1075 women met this criterion using the backward-counting method). Again, none of these analyses revealed any significant effects of progesterone. Full results of these robustness- check analyses are available on the Open Science Framework (https://osf.io/9fqcm/).

Additional Analyses

In addition to the analyses described above, we tested for simple correlations between estimated progesterone and pathogen disgust in the full sample (Table 5), as well as for samples with the two more stringent inclusion criteria described in our robustness checks. Results of the robustness analysis are given on the Open Science Framework (https://osf.io/9fqcm/).

We also compared pathogen disgust in the luteal phase of the menstrual cycle (backward-counting method: -1 to -13, forward-counting: 16 to 39) and follicular phase (backward-counting: -14 to -34, forward-counting: 6 to 15) using independent samples t-tests. These analyses were modelled on those reported by Miłkowska et al. (2021). The outcome of the independent t-test indicates no significant difference between pathogen disgust in the follicular versus luteal phase ($t_{backward-counting} = -1.70$, $df = 1247.1$, $p = 0.089$, $t_{forward-counting} = -0.87$, $df = 938.14$, $p = 0.386$). Full results of these analyses including robustness analysis are available on the Open Science Framework (https://osf.io/9fqcm/).

Discussion

Our between-subjects analyses of disgust sensitivity showed no evidence that pathogen disgust increases on days of the menstrual cycle when progesterone is high. These null results are consistent with null results for progesterone and pathogen disgust reported in recent studies that used longitudinal designs to investigate whether pathogen disgust tracks changes in progesterone (Jones et al., 2018; Stern & Shiramizu, 2022) and do not support the Compensatory Prophylaxis Hypothesis.

Bressan and Kramer (2022) recently suggested that carry-over effects when pathogen disgust is assessed repeatedly in longitudinal studies might obscure progesterone-linked changes in pathogen disgust and suggested the null results reported in these longitudinal studies should be interpreted cautiously. In the current study, we observed null results for progesterone and pathogen disgust in a between- subjects analyses where there was no opportunity for such carry-over effects to occur. That we observed null results using a between-subjects design suggests that the absence of significant associations between progesterone and pathogen disgust in recent studies is unlikely to be a consequence of carry-over effects having obscured progesterone-linked changes in pathogen disgust.

Although we used a between-subjects design in the current study specifically to explore the possibility that progesterone-linked changes in pathogen disgust are only evident in studies that are not subject to such carry-over effects (i.e., those that do not require repeated testing of individual participants), we acknowledge that between-subjects designs are suboptimal for testing the Compensatory Prophylaxis Hypothesis. Consequently, we strongly recommend that future work on this topic use longitudinal designs. Ideally such studies would also employ well-validated objective measures of progesterone levels (e.g., the liquid chromatography mass spectrometry method used by Stern and Shiramizu, 2022), rather than imputed values or progesterone measured from saliva samples via immunoassay. We also note here that future studies on this topic might also benefit from employing measures of pathogen disgust other than the explicit responses to questionnaires that are typically used in work on this topic. For example, we do not discount the possibility that studies employing psychophysiological measures of disgust (see De Smet et al., 2014) in response to pathogen-related and control images (e.g., those developed by Curtis et al., 2004) might yet reveal compelling evidence for the Compensatory Prophylaxis Hypothesis. Such studies might also consider factors such as recent experience of infectious illness, which some previous work suggests might moderate the effects of progesterone on disgust sensitivity (Milkowska et al., 2019; but see also Stern & Shiramizu, 2022). Relatedly, we also acknowledge the possibility that the null results reported in the current study may be false negatives. Imprecision in both estimates of progesterone levels and measurement of disgust sensitivity could still result in low statistical power, despite the large sample size in our study.

Where questionnaires are used to assess pathogen disgust it may be beneficial to use questionnaires that are optimized for assessing current (i.e., state) disgust sensitivity. Tybur et al.'s (2009) Three Domain Disgust Scale, the disgust sensitivity measure used in the current study, may be better suited to measuring trait-like aspects of disgust. However, we note here that Miłkowska et al. (2021) have previously reported increases in pathogen disgust during the luteal phase of the menstrual cycle when pathogen disgust was measured using the pathogen disgust subscale of the Three Domain Disgust Scale, the contamination subscale of the Revised Padua Obsessive-Compulsive Inventory, and disgust ratings of images depicting pathogen cues. Miłkowska et al's (2021) results then suggest that Tybur et al.'s (2009) Three Domain Disgust Scale may not necessarily be inappropriate for testing the Compensatory Prophylaxis Hypothesis.

Curtis et al., (2004) have previously reported age-related decline in pathogen disgust when pathogen disgust was assessed via ratings of pathogen-related images. By contrast, we did not observe a significant negative relationship between age and pathogen disgust assessed via the Three Domain Disgust Scale. However, we did observe significant relationships between age and both moral disgust (positive relationship) and sexual disgust (negative relationship). These results suggest age may have different effects on different components of disgust sensitivity.

Conclusion

In conclusion, we used a between-subjects design to test for a positive relationship between imputed progesterone levels and pathogen disgust assessed using the Three Domain Disgust Scale. In contrast with the recent proposal that carry-over effects when women's pathogen disgust is tested repeatedly might obscure progesterone-linked increases in pathogen disgust (Bressan & Kramer, 2022), we observed no significant relationships between pathogen disgust and progesterone. Our null results then add to a growing body of work (Jones et al., 2018; Stern & Shiramizu, 2022) whose results have not supported the Compensatory Prophylaxis Hypothesis.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40750-022-00208-5.

Acknowledgements We thank Roger Mundry for providing the R script for model diagnostics. We also acknowledge support from the Open Access Publication Funds of Göttingen University. We further thank the German Academic Exchange Service (DAAD).

Authors' Contributions The study was conceptualized by Y.R., B.C.J., and V.S. Y.R. processed and analyzed the data with input from V.S and B.C.J. The manuscript was drafted by Y.R. and B.C.J. All authors contributed by commenting and revising the final manuscript.

Funding This work was supported by Deutsche Forschungsgemeinschaft, Grant/Award Number: 254142454 / GRK 2070.
Open Access funding enabled and organized by Projekt DEAL.

Data Availability The data and statistical analysis used in the current study are publicly available on Open Science Framework (OSF): https://osf.io/9fqcm/.

Author Note The preprint was published in PsyArXiv: https://psyarxiv.com/9fsgq/.

Declarations

Ethical Approval The project was approved by the School of Psychology, University of Glasgow, Ethics Review Board.

Competing Interest None.

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