

## Hormonal predictors of sexual motivation in natural menstrual cycles

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### ABSTRACT

Little is known regarding which hormonal signals may best predict within- and between-women variance in sexual motivation among naturally cycling women. To address this, we collected daily saliva samples across 1–2 menstrual cycles from a sample of young women; assayed samples for estradiol, progesterone, and testosterone; and also collected daily diary reports of women's sexual behavior and subjective sexual desire. With respect to within-cycle, day-to-day fluctuations in subjective desire, we found evidence for positive effects of estradiol and negative effects of progesterone. Desire exhibited a mid-cycle peak, similar to previous findings; measured progesterone concentrations statistically mediated the fall in desire from mid-cycle to the luteal phase, but no combination of hormone measures substantially mediated the follicular phase rise in desire, which suggests that other signals may be implicated in this effect. Hormonal predictors of within-cycle fluctuations in sexual behavior generally reached only trend levels of statistical significance, though the patterns again suggested positive effects of estradiol and negative effects of progesterone. Between-women and within-women, between-cycle effects of hormone concentrations were generally absent, although statistical power was more limited at these higher levels of analysis. There were no significant effects of testosterone concentrations when controlling for the effects of estradiol and progesterone, which raises questions regarding the importance of this hormone for the regulation of sexual motivation in natural cycles. Our study is among the first to identify hormonal predictors of within-cycle fluctuations in sexual motivation, and thus adds novel evidence regarding the endocrine correlates of human sexuality.

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### Introduction

Surprisingly little research has directly addressed the hormonal predictors, if any, of women's sexual motivation in natural menstrual cycles (Stuckey, 2008; Wallen, 2001). Although non-hormonal factors undoubtedly play crucial roles in determining women's sexual motivation (e.g., Bodenmann et al., 2010; Dennerstein et al., 2005), various lines of evidence support a significant role for sex hormones as well. Sexual motivation tends to drop after natural or surgical menopause (Alexander et al., 2004; Dennerstein et al., 1977, 2005; Gracia et al., 2007); a number of studies have reported increased sexual desire or behavior near ovulation, which implicates a role for ovarian hormones (e.g., Adams et al., 1978; Bullivant et al., 2004; Dennerstein et al., 1994; Diamond and Wallen, 2011; Harvey, 1987; Matteo and Rissman, 1984; Pillsworth et al., 2004; Stanislaw and Rice, 1988; Wallen, 2001; Wilcox et al., 2004; cf. Regan, 1996; Schreiner-Engel and Schiavi, 1981); the chemical suppression of ovarian hormones in a sample of naturally cycling women led to large drops in sexual motivation (Schmidt et al., 2009); and evidence supports the efficacy of hormone replacement

therapy in increasing sexual motivation in menopausal women via use of various doses of estrogen (Dennerstein et al., 1980; Nathorst-Boos et al., 1993; Sherwin, 1991; Wiklund et al., 1993), testosterone added to estrogen (Braunstein et al., 2005; Floter et al., 2002; Sherwin et al., 1985), or testosterone alone (Davis et al., 2008).

Despite the above evidence for hormonal influences, there is as of yet no clear model of the specific hormonal signals associated with within- and between-women variance in sexual motivation within natural menstrual cycles. Only a handful of studies (Dennerstein et al., 1994; Morris et al., 1987; Persky et al., 1978a,b; Van Goozen et al., 1997) have measured hormone concentrations across broad regions of the menstrual cycle in order to test for associations with measures of libido in premenopausal women. The only significant findings reported in these studies have been positive, between-women correlations between average or mid-cycle testosterone and some measures of sexual frequency (Morris et al., 1987; Persky et al., 1978b; Van Goozen et al., 1997; cf. Bancroft et al., 1983). No studies have reported significant associations between within-women, day-to-day fluctuations in hormones and changes in sexual thoughts or behaviors, which leaves unknown the physiological signals that may regulate cyclic patterns of libido.

The conclusiveness of the above studies that have tested hormonal correlates of sexual motivation is limited, however, by significant methodological issues. Most of the studies were underpowered, and did not exploit the power that can be gained from analyzing nested data via

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mixed-level regression modeling; hormone sampling was typically infrequent (usually 2–3 times per week; cf. Van Goozen et al., 1997); only univariate analyses were performed, with no studies having tested the partial effects of hormones while controlling for the effects of others; and, finally, only same day associations between hormones and dependent measures have been assessed, despite possible time delays for genomic effects of some hormones (see below). Summing up the limitations of this literature, Wallen (2001) wrote: "... after more than 30 years of study, there is still no human study that has correlated daily changes in ovarian hormones with daily ratings of sexual desire and looked at both estrogens and androgens" (p. 352). The present study was designed in part to address this gap in the human literature.

Here we collected daily saliva samples across 1–2 menstrual cycles from a sample of naturally cycling young women, as well as daily diary reports of both sexual behavior and self-reported sexual desire. Saliva samples were assayed for estradiol, testosterone, and progesterone every day across a nine day window surrounding the estimated day of ovulation (see *Methods* section), and on alternating days outside of this window. Mixed model regression analyses were employed, allowing tests of within-cycle (Level-1) predictors of sexual motivation (e.g., do day-to-day fluctuations in estradiol predict within-cycle fluctuations in libido?); within-women, between-cycle (Level-2) predictors (e.g., does change in average estradiol across the same woman's two cycles predict change in her average sexual motivation?); and between-women (Level-3) predictors (e.g., do women with higher estradiol on average also experience higher sexual motivation on average?). Previous studies have sometimes confounded these three sources of variance, and no studies have systematically examined all three levels of analysis within the same sample.

We hypothesized that estradiol would positively predict within-cycle; between-cycle, within-women; and between-women variance in sexual motivation. Estradiol indexes within-cycle fertility since it peaks near ovulation, but also indexes between-cycle fertility given evidence that conception is more likely in cycles with higher estradiol (Lipson and Ellison, 1996; Venners et al., 2006). We have proposed elsewhere (Roney, 2009; Roney and Simmons, 2008) on functional grounds the existence of mechanisms that calibrate mating motivation to fluctuations in fertility, and the direct links between estradiol and fertility thus make this hormone a logical signal to regulate this calibration. Progesterone, by contrast, could promote within-cycle links between fertility and sexual motivation by acting as an inhibitory signal that reduces libido during the non-fertile luteal phase, but such effects could undermine between-cycle calibration of motivation to fertility since progesterone concentrations tend to be higher in more fertile cycles characterized by favorable energetics (for review, see Ellison, 2001); if there were fitness advantages to the up-regulation of sexual motivation even during the luteal phases of more vs. less fertile cycles (e.g., as a means of allocating greater attention to mate search, or to signal paternity confidence to a partner via greater sexual activity), then progesterone may have been a suboptimal regulatory signal. The consistent, positive correlation between estradiol and fertility at both within- and between-cycle time-scales, on the other hand, suggests its potential efficiency as a regulator of sexual motivation. In addition to these theoretical considerations, estradiol is known to promote various aspects of sexual motivation among both rodents (e.g., Carter, 1992; Pfaff et al., 2002) and nonhuman primates (e.g., Wallen et al., 1984; Zehr et al., 1998), although some evidence in primates suggests inhibitory effects of progesterone (e.g., Wallen et al., 1984), as well.

In assessing within-cycle predictors of sexual motivation, it is potentially important to account for possible time delays in the effects of ovarian hormones. Estradiol appears to affect sexual receptivity in female rodents at a lag of approximately two days (with effects decaying rapidly beyond two days without further doses of estrogen), whereas progesterone has effects within minutes to hours (Blaustein, 2008; Powers, 1970; Whalen, 1974). To assess possible time delays, we tested the effects of current day, one day lag, and two day lag hormone concentrations, and,

based on the rodent findings, specifically hypothesized that estradiol concentrations from two days earlier will positively predict indices of women's current day sexual motivation. Although our a priori expectation was that estradiol would be the crucial signal, our design allowed tests for effects of testosterone and progesterone as well. Finally, our design also allowed us to add time variables (proximity to ovulation, weekend timing) to models that included hormonal predictors.

## Methods

### Participants

Women were recruited from a subject pool website run by the Department of Psychology at UCSB. Pregnancy, lactation, or any use of hormonal contraceptives within the last six months were exclusion criteria, as were self-reported menstrual cycles longer than 40 days. Fifty-two eligible women enrolled in the study and completed data collection for the first menstrual cycle. Of these women, 37 returned for a second cycle ( $n = 7$  declined to continue,  $n = 2$  transferred schools,  $n = 1$  started taking hormonal contraceptives,  $n = 2$  were not invited back due to poor compliance in cycle 1,  $n = 1$  dropped out after initially starting cycle 2, and  $n = 2$  failed to menstruate within five weeks of the start of cycle 2 data collection). Hormones were assayed from 43 of the women in cycle 1 (to save costs, we did not assay hormones from 9 of the cycle 1 women who did not return for cycle 2, but assayed hormones from 6 of the women who did not return but had high rates of compliance in cycle 1), and from 36 of 37 women in cycle 2 (one woman with many missing samples was excluded from the assays); as such, we obtained hormone data from 43 total women, with 36 contributing two cycles of data and 7 contributing one. Mean age of these 43 women was  $18.76 \pm 1.15$  years, and all self-reported a heterosexual orientation. Fourteen of the 43 women reported that they were within a romantic relationship in cycle 1, whereas 10 out of 36 women reported being in a relationship during cycle 2. Women were paid \$100 per cycle if they missed fewer than three daily log-in sessions in a given cycle, and were paid lower, pro-rated amounts if they had more missing data. Participants provided written, informed consent for their participation, and all procedures were in accordance with the Code of Ethical Principles for Medical Research Involving Human Subjects of the World Medical Association (Declaration of Helsinki).

### Procedure

Women participants were first directed to a secure website on which they indicated daily whether they had started a new menstruation; upon an affirmative answer, they were directed to a new link and instructed to complete the survey found there each morning until the end of their cycle (women also indicated in that survey whether bleeding occurred on each response day). This survey included the items that comprise the dependent variables in the present report. Subjective desire was measured via the item: "How much did you desire sexual contact yesterday?" (1–7 scale). Our primary behavioral dependent variable read as follows: "Did you engage in sexual activity (intercourse or other forms of genital stimulation) with another person yesterday?" (Y/N). Because sexual behavior may occur in response to partners' desires and thus imperfectly index sexual motivation, we also examined two secondary behavioral variables. In cases in which sex occurred, women were also asked: "Who initiated the sexual activity? (You, Other person, Both)." Our initial intention was to analyze cases initiated exclusively by the woman, but there were too few such cases—a total of 15 across the entire study—to do so. Instead, we computed a measure of woman-initiated sexual behavior that was coded 1 if sex occurred and the woman indicated that she or both she and her partner had initiated it, and was coded zero otherwise. The final behavioral measure assessed autosexual behavior: "Did you engage in self-stimulation (masturbation) yesterday?" Because the items referred

to “yesterday,” responses were aligned with hormone concentrations from the previous day.

Women were also instructed to collect a saliva sample each morning. They were asked to do so at least 30 min after any eating or drinking, ideally upon first waking. Collection was via passive drool (a few minutes after rinsing with clean water) into pre-labeled polypropylene vials. Women stored these vials in home freezers and then delivered them weekly to our research lab, at which time they were given a new batch of vials. Saliva samples were then stored at  $-80\text{ C}$  until being shipped for assay. The same procedures described above were repeated in cycle 2 for those women who returned for a second cycle; the two cycles were separated by 1–2 months.

### *Hormone assays*

Saliva samples were shipped on dry ice to the Endocrine Core Laboratory at the California Regional Primate Research Center, Davis, CA. Samples were centrifuged at 3000 rpm for 20 min. to separate the aqueous component from other particles. Concentrations of progesterone were estimated in duplicate using commercial radioimmunoassay kits (Siemens Health Diagnostics, Inc., Los Angeles, CA). Assay procedures were modified to accommodate overall lower levels of progesterone in human saliva relative to plasma as follows: 1) standards were diluted to concentrations ranging from 0.05 to 4.0 ng/mL; and 2) sample volume was increased to 200  $\mu\text{l}$ . The progesterone assay has a least detectable dose of 0.00914 ng/ml; intra- and inter-assay CVs were 4.57% and 7.36%, respectively. Concentrations of testosterone were estimated in duplicate using double-antibody commercial radioimmunoassay kits (Beckman Coulter Inc., Webster, TX.). The assay procedures were those outlined in Granger et al. (1999). The testosterone assay has a least detectable dose of 1.3697 pg/ml; intra- and inter-assay CVs were 5.20% and 9.83%, respectively. Estradiol concentrations were estimated in duplicate using the high sensitivity salivary  $17\beta$ -estradiol enzyme immunoassay kit (Salimetrics LLC, State College, PA). The estradiol assay has a least detectable dose of 0.1 pg/ml; intra- and inter-assay CVs were 4.52% and 8.15%, respectively.

### *Data analyses*

#### *Cycle phase estimation*

Prior to shipping saliva for assay, we estimated the day of ovulation as 15 days prior to the end of each cycle. All saliva samples in a nine day window centered on this day were sent for assay, as well as samples from alternating days outside of this window ( $N = 3621$  total assays). We then used the hormone data to re-estimate the day of ovulation based on the conjunction of the mid-cycle estradiol drop and the initiation of the luteal phase progesterone increase (see Gann et al., 2001; Lipson and Ellison, 1996): we computed a three day moving average for progesterone concentrations and then assigned the day of ovulation (day zero) as the day with the largest drop in estradiol from the previous day that occurred within two days of a 20% or greater increase in the moving average for progesterone, conditional on this day being followed by a sustained elevation in progesterone (for cycles without sustained progesterone elevations—see below—we designated day zero as the day with the largest drop in estradiol that occurred near mid-cycle). The “fertile window” (i.e. cycle days when conception is possible) was then defined as the estimated day of ovulation and the preceding five days (Wilcox et al., 1998); the follicular phase was defined as ending on the day of ovulation, with all subsequent days defined as luteal. Note that ovulatory timing was primarily used for graphical purposes, and only affected statistical tests that included the fertile window variable; the main tests of hormonal predictors of sexual motivation directly assessed associations between measured hormone concentrations and outcome variables and did not rely on the accuracy of ovulatory timing estimation.

Because a fertile window exists only in ovulatory cycles, the fertile window analyses were restricted to the set of cycles judged ovulatory. Following Ellison et al. (1987), we defined as anovulatory any cycle that did not achieve a maximum progesterone value of at least 300 pmol/L; this criterion identified 53 out of 79 total cycles as ovulatory (33% anovulatory, compared to 41% among undergraduates in Ellison et al., 1987). This was likely a conservative criterion for ovulation that may have classified some ovulatory cases of luteal insufficiency as anovulatory, but had the advantage of employing an objective cut-off point that ensured that the fertile window analyses were truly restricted to ovulatory cycles. Our primary regression analyses testing hormonal predictors of sexual motivation included all cycles, since hormone concentrations may still predict outcomes in anovulatory cycles, and because cycles with smaller hormone fluctuations provide data relevant to the computation of the overall effects of hormone fluctuations across all cycles.

#### *Outlier removal*

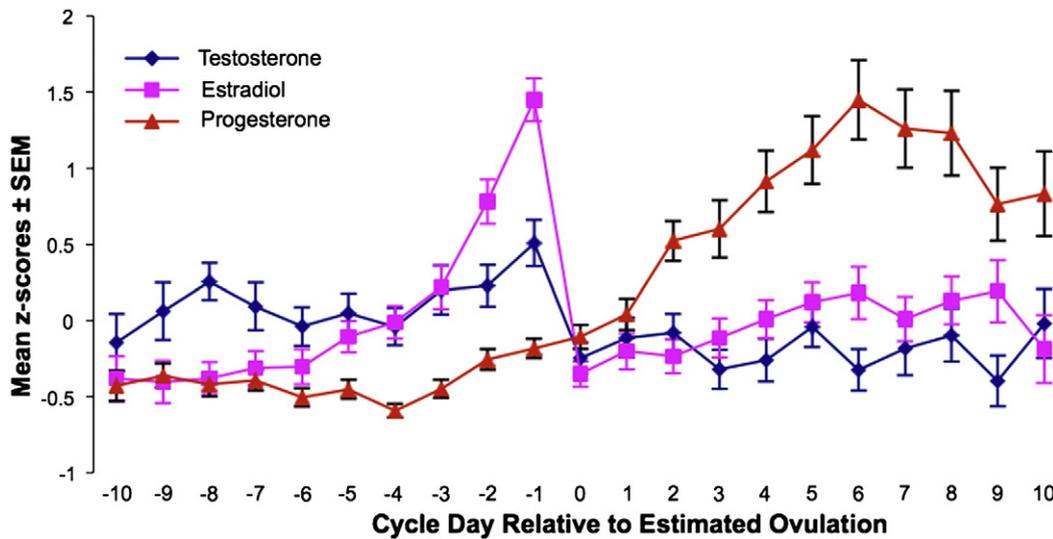
We identified hormone outliers in a phase-specific manner by dividing the cycle into bins relative to the estimated day of ovulation (day 0): days  $-10$  to  $-7$ ,  $-6$  to  $-4$ ,  $-3$  to  $-1$ ,  $0$  to  $+1$ ,  $+2$  to  $+4$ ,  $+5$  to  $+7$ ,  $+8$  to  $+10$ , and all days outside of  $-10$  to  $+10$ ; hormone values greater than 3 SD from the respective bin-specific means were then removed (although no statistical conclusions were altered by inclusion of the outliers). This procedure avoids misidentifying phase-specific peaks (e.g., the pre-ovulatory estradiol peak) as outliers relative to the grand mean. Outliers comprised 1.4%, 1.7%, and 1.5% of estradiol, progesterone, and testosterone values, respectively.

#### *Statistical models*

Our analysis strategy employed mixed regression models in SPSS v19: these models are ideally suited for the analysis of nested data with correlated error terms (Raudenbush and Bryk, 2002). In the present case, daily variables (Level-1) were nested within cycles (Level-2), which were nested within women (Level-3). Hormone concentrations were first z-scored so that all three hormones were placed on the same scale. Separate models were constructed at Level-1 to test the within-cycle effects of current day hormones, hormones measured one day before the response day, and hormones measured two days before the response day (missing data for days without assays precluded entering all time lags into the same model); hormone concentrations were group-mean centered in these models, such that the intercepts represent estimated values for the dependent variables when hormones were at their respective cycle means. We constructed separate mixed regression models to test Level-2 (within-women, between-cycle) and Level-3 (between-women) effects of hormones. At Level-2, for the set of women with two cycles of hormone data ( $n = 36$ ), we centered mean hormone concentrations within each cycle relative to each woman's overall mean and then entered these scores into mixed regression models: as such, these models assessed whether changes in mean hormone concentrations within-women, between-cycles predicted changes in the intercepts of the dependent variables across the two cycles. At Level-3, we entered women's mean hormone concentrations across the entire study into mixed regression models in order to test whether women with higher overall hormone concentrations also scored higher on the dependent measures. Equations for the mixed models appear in Appendix A. A first-order autoregressive error structure was specified at Level-1 to account for autocorrelation in the dependent measures. Linear mixed models were employed for the continuous measure of desire for sex, but mixed binary logistic models were used for the dichotomous sexual behavior variables.

### **Results**

A total of 1905 daily log-in responses were obtained from the 43 women with hormone data out of 2079 eligible cycle days, for an overall compliance rate of 91.6%. After selection of saliva samples from



**Fig. 1.** Mean testosterone, estradiol, and progesterone concentrations aligned against estimated day of cycle (day 0 represents the estimated day of ovulation) and aggregated across all women. Values are standardized with respect to the grand means. Error bars are  $\pm$  SEM.

alternating days outside of mid-cycle, and after outlier removal, measured hormone concentrations were available for 1181, 1179, and 1208 of the log-in days for estradiol, progesterone, and testosterone, respectively. Mean hormone concentrations aggregated across women and aligned against day of cycle reproduced prototypical hormone curves (Fig. 1), thus providing evidence for validity of the hormone assays. Table 1 demonstrates that the three hormone concentrations were all positively correlated with one another within-cycles, whereas mean testosterone and mean estradiol concentrations were positively correlated between-women.

*Sexual desire*

*Within-cycle analyses*

Table 2 presents results of mixed regression models testing the effects of all three hormones on sexual desire at three different time-scales; because visual inspection of the data revealed a strong positive effect of weekend timing (defined as Friday or Saturday), a binary weekend timing variable was also included in each of the models. Progesterone was a significant negative predictor of desire in all three models, with the strongest effects observed at a two day time lag. Estradiol measured two days earlier was a significant positive predictor of sexual desire, and current day estradiol exhibited a trend toward a positive effect. There were no effects of testosterone at any time-scale in the full models; a positive zero-order effect of testosterone at a two day lag ( $\gamma = 0.11$ ,  $p = 0.047$ ) dropped out when estradiol was added to the model, suggesting that this effect was an artifact of the positive within-cycle correlation between these hormones (see Table 1). Weekend timing had a significant positive effect in all three models, but was independent of the effects of hormone concentrations as removal of this variable

produced negligible changes in the parameter estimates for the hormone variables, and vice-versa. There were no significant interactions between any of the predictor variables in Table 2.

We next examined the effect of fertile window timing on sexual desire (only ovulatory cycles were included in these analyses). When considering all cases for which desire ratings were available, the zero-order, within-cycle relationship between fertile window timing and desire for sex was significant,  $\gamma = 0.26$ ,  $p = 0.023$ , with greater desire inside the estimated fertile window (mean =  $3.74 \pm 0.20$ ) than on other days (mean =  $3.48 \pm 0.18$ ). Fig. 2 plots desire ratings against day of the cycle (the progesterone curve is included in order to visually depict the relationship between progesterone and desire); the highest mean desire ratings occurred on the estimated day of ovulation, and a clear drop in desire was evident in the luteal phase beginning on post-ovulatory day five. A positive effect of fertile window timing was found both when analyses were restricted to follicular phase days,  $\gamma = 0.32$ ,  $p = 0.012$ , and when restricted to fertile window plus luteal phase days,  $\gamma = 0.28$ ,  $p = 0.027$ , which demonstrates that the effect included both a rise in desire from the early to late follicular phase and a fall in desire from the late follicular phase to the luteal phase.

The results presented in Table 2 in conjunction with the fertile window analyses suggest the possibility that the follicular phase rise in desire may be mediated by increasing estradiol concentrations, whereas the luteal phase drop in desire may be mediated by elevated progesterone. When analyses were restricted to fertile window plus luteal phase days for those days on which hormone assays were available, the zero-order effect of fertile window timing was  $\gamma = 0.29$ ,  $p = 0.064$ . Addition of current day progesterone to this model reduced the fertile window effect to  $\gamma = 0.03$ ,  $p = 0.85$  (progesterone effect:  $\gamma = -0.19$ ,  $p = 0.008$ ), whereas addition of estradiol or testosterone as the only other predictor had negligible effects on the parameter estimates for fertile window timing ( $\gamma$ s = 0.28 and 0.32, respectively); similar evidence for exclusive mediation by progesterone was found for the one and two day lag hormone models. When analyses were restricted to the follicular phase, the zero-order effect of fertile window timing for those days with hormones measured two days earlier (since the two day lag model included the only significant estradiol effect; see Table 2) was  $\gamma = 0.35$ ,  $p = 0.032$ . Addition of two day lag estradiol to this model caused only a small drop in the magnitude of the fertile window effect,  $\gamma = 0.28$ ,  $p = 0.094$ ; likewise, neither addition of the other individual hormones nor any combination of hormones caused a substantial drop in the size of the fertile window coefficient. Similar lack of mediation was found

**Table 1**  
Correlations between hormone concentrations.

	Estradiol	Progesterone	Testosterone
Estradiol			
Progesterone	.21**	.11	.38*
Testosterone	.35**	.15**	.03

Note. Values below the diagonal are within-cycle correlations (hormone concentrations were standardized within-cycles, then correlated across all data points); values above the diagonal are between-women correlations (subject mean hormone values were correlated with each other).

\*\*  $p < 0.01$ .  
\*  $p < 0.05$ .

**Table 2**  
Mixed regression models testing within-cycle predictors of desire for sex.

	2-day lag		1-day lag		Current day	
	$\gamma$ (df)	<i>p</i> -value	$\gamma$ (df)	<i>p</i> -value	$\gamma$ (df)	<i>p</i> -value
Intercept	3.54 (44)	<0.001	3.51 (43)	<0.001	3.52 (44)	<0.001
Progesterone	<b>−0.20 (503)</b>	<b>0.0001</b>	<b>−0.11 (501)</b>	<b>0.04</b>	<b>−0.13 (584)</b>	<b>0.01</b>
Estradiol	<b>0.16 (824)</b>	<b>0.01</b>	0.05 (862)	0.37	0.09 (888)	0.096
Testosterone	0.07 (797)	0.20	0.02 (843)	0.69	−0.07 (888)	0.22
Weekend	<b>0.35 (808)</b>	<b>0.0002</b>	<b>0.39 (843)</b>	<b>&lt;0.0001</b>	<b>0.40 (875)</b>	<b>&lt;0.0001</b>

Note. Hormone variables were standardized (relative to their respective grand means) and then group-mean centered within-cycles; as such, coefficients represent the within-cycle change in sexual desire associated with a 1 SD change in hormone concentrations. Weekend was dummy coded. *DF* reflects the Satterthwaite correction as generated by the SPSS program. Bold font highlights statistically significant predictors.

when testing the effects of one day lag and current day hormones; this absence of mediation also persisted if we excluded day 0 (a low estradiol day) from our definition of the fertile window. In sum, we found that the drop in desire from the fertile window to the luteal phase was statistically mediated by measured progesterone concentrations, but were unable to demonstrate substantial hormonal mediation of the rise in desire during the follicular phase.

#### Within-women, between-cycle analyses

A mixed regression model for those women with two cycles of hormone data ( $n = 36$ ) tested the within-women effects of cycle mean estradiol, testosterone, and progesterone on mean sexual desire across the two cycles. There were no significant effects, but the coefficient for mean estradiol was negative,  $\gamma = -0.33$ ,  $p = 0.12$ , contrary to our prediction. As an intuitive check on these results, we also computed correlations between within-women changes in mean hormone concentrations and within-women changes in mean desire; no effects were significant. The correlation for estradiol was  $r = -0.24$ ,  $p = 0.15$ ; approximately 68 subjects would be necessary to detect this effect size as statistically significant. There were no interactions between the cycle mean hormone concentrations in the prediction of sexual desire (all  $ps > 0.30$ ).

Restricted variance within-women, between-cycles may help explain the null effects at this level of analysis. Only 2.7% of the variance in sexual desire was within-women, between-cycles, for example, whereas 31.4% was between-women and 65.9% was within-cycles. Likewise, 10.7, 14.2, and 2.6% of the variance in estradiol, testosterone, and progesterone, respectively, was within-women, between-cycles; this similarity in hormone concentrations across cycles within the same women may

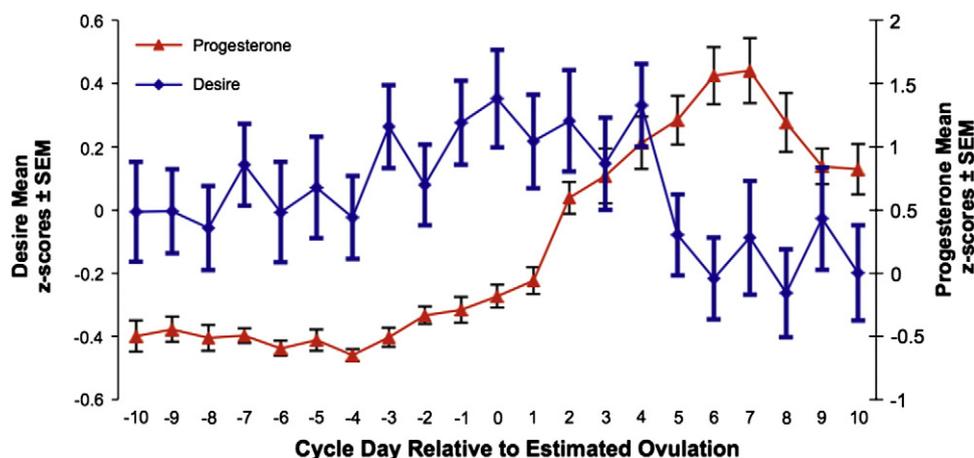
have limited our ability to detect reliable effects at the between-cycle time-scale.

#### Between-women analyses

Subjects' mean concentrations of estradiol, testosterone, and progesterone over the full study were entered as predictors of sexual desire in a mixed regression model; there were no significant effects (all  $ps > 0.20$ ). A multiple regression analysis with subject mean desire regressed onto subject mean hormones provides essentially the same information, but may be more intuitive for some readers. This analysis produced the following standardized regression coefficients for the three hormones: for estradiol,  $\beta = 0.21$ ,  $p = 0.22$ ; for testosterone,  $\beta = 0.10$ ,  $p = 0.57$ ; for progesterone,  $\beta = -0.10$ ,  $p = 0.53$ . There were no significant interactions between the three mean hormone variables in the prediction of desire (all  $ps > 0.10$ ).

#### Sexual behavior

The within-women (Level-1) and within-women, between-cycle (Level-2) analyses for the sexual behavior variables were restricted to the subsets of women who reported nonzero frequencies of the respective behaviors, since there was otherwise no variance to explain at Level-1 or Level-2 (between-women analyses included all women). A total of 178 episodes of sexual behavior with a partner were reported across 29 women; among these episodes, 85 involved female initiation, distributed across 21 of the sexually active women. One hundred thirty-two of the 178 cases of sexual behavior occurred among women who reported that they were currently in a relationship; relationship status



**Fig. 2.** Mean desire for sex and mean progesterone concentrations aligned against estimated day of cycle (day 0 represents the estimated day of ovulation) for the set of ovulatory cycles. Desire values are standardized within-cycles such that zero on the primary y-axis represents the mean desire for sex within a given cycle. Error bars are  $\pm$  SEM.

**Table 3**  
Mixed regression models testing within-cycle predictors of sexual behavior.

	2-day lag		1-day lag		Current day	
	$\gamma$ (Exp <i>b</i> ) ( <i>n</i> = 586)	<i>p</i> -value	$\gamma$ (Exp <i>b</i> ) ( <i>n</i> = 621)	<i>p</i> -value	$\gamma$ (Exp <i>b</i> ) ( <i>n</i> = 642)	<i>p</i> -value
Progesterone	-0.09 (0.92)	0.47	0.02 (1.02)	0.87	0.02 (1.02)	0.87
Estradiol	0.17 (1.19)	0.23	0.02 (1.02)	0.91	<b>0.30 (1.34)</b>	<b>0.02</b>
Testosterone	0.19 (1.21)	0.18	0.15 (1.16)	0.32	-0.05 (0.95)	0.76
Weekend	<b>1.10 (3.01)</b>	<b>&lt;0.0001</b>	<b>0.67 (1.95)</b>	<b>0.01</b>	<b>1.15 (3.17)</b>	<b>&lt;0.0001</b>

Note. Hormone variables were standardized (relative to their respective grand means) and then group-mean centered within-cycles; as such, coefficients represent the within-cycle change in the odds ratio for sexual behavior (Exp *b*) associated with a 1 SD change in hormone concentrations. Weekend was dummy coded. Bold font highlights statistically significant predictors.

did not interact with any of the other predictor variables in the mixed regression models, and thus the sexual behavior analyses were collapsed across single and partnered women. A total of 186 episodes of masturbation were reported, distributed across 23 women.

*Within-cycle analyses*

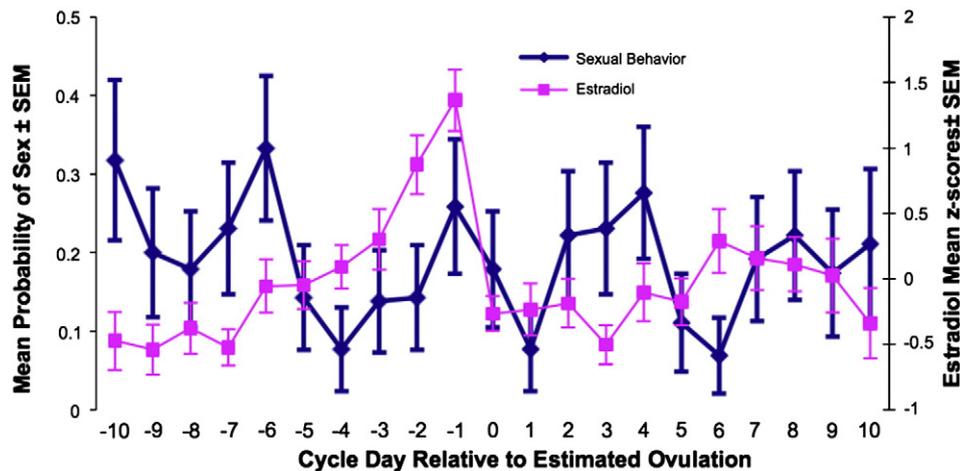
Mixed model binary logistic regression was employed to model the probability of sexual behavior (i.e. genital contact with another person) on a given day for the set of women with hormone data who reported any sex (*n* = 29). Table 3 presents models testing the effects of hormones measured the same day, one day earlier, and two days earlier. There was a significant effect of current day estradiol: for each one standard deviation increase in estradiol, the odds of sexual behavior increased by 34% relative to other days in the same cycle. No other main effects of hormones were significant, although there was a positive interaction between current day testosterone and progesterone (*p* = 0.013) such that progesterone had more positive effects when testosterone was high than when testosterone was low; given the number of interactions tested in an exploratory manner, though, this effect should be interpreted with caution. Weekend timing was a strong, positive predictor of sexual activity in all three models; considered across all cases (i.e. whether or not hormone data were available on a given day), the probability of sex on weekend days was 22% versus 9% on other days. As with sexual desire, the effects of weekend timing were independent of the effects of hormone concentrations.

The same models depicted in Table 3 were re-run with woman-initiated sex as the dependent variable, which restricted the analysis to a subset of the sexual behavior events. These models identified only two trends among the hormone variables: a positive effect for current day estradiol ( $\gamma$  = 0.35, *p* = 0.08, Exp *b* = 1.43), and a negative effect for current day progesterone ( $\gamma$  = -0.45, *p* = 0.06, Exp *b* = 0.64). Similarly, when masturbation was entered as the dependent variable (analyses were restricted to the 23 women who reported any

masturbation), a trend toward a positive effect of current day estradiol ( $\gamma$  = 0.28, *p* = 0.06, Exp *b* = 1.33) was the only result that approached significance.

Whether a response day fell within the fertile window did not predict the odds of sexual contact, woman-initiated sexual contact, or masturbation (all *ps* > 0.10). Fig. 3 plots the mean probability of sexual contact by cycle day; mean estradiol concentrations are also depicted, given the positive relationship between current day estradiol and odds of sex (see Table 3). Visual inspection of the figure suggests the absence of any clear mid-cycle peak in sexual frequency.

On the recommendation of a reviewer, we also examined whether menstrual bleeding or premenstrual timing affected the within-cycle prediction of sexual behavior; in principle, hormone effects could be artifacts of avoidance of sexual activity due to discomfort associated with these events. Dummy variables were created indicating whether a woman reported bleeding on a given response day, and whether a response day was one of the last four days before onset of next menses. These variables were first entered into mixed regression models that included weekend timing but not the hormone variables: premenstrual timing did not significantly predict any of the sexual behavior variables; menstrual bleeding was associated with lower odds of sexual behavior with a partner ( $\gamma$  = -1.26, *p* = 0.001, Exp *b* = 0.28), and with lower odds of woman-initiated sexual contact ( $\gamma$  = -1.14, *p* = 0.016, Exp *b* = 0.32). Addition of these variables to the models that tested the within-cycle effects of hormone concentrations, however, had minimal effects on the coefficients for the hormone variables: the only statistical conclusion altered by the addition of these terms was the marginally significant effect of estradiol on the odds of masturbation (see above), which became statistically significant ( $\gamma$  = 0.35, *p* = 0.024, Exp *b* = 1.42), although even in this case the change in odds ratio was small. The significant effect of current day estradiol on the probability of sexual behavior with a partner was basically unaffected by addition of these variables ( $\gamma$  = 0.31, *p* = 0.022, Exp *b* = 1.36;



**Fig. 3.** Mean probability of sexual contact and mean estradiol concentrations aligned against estimated day of cycle (day 0 represents the estimated day of ovulation) for the set of ovulatory cycles in which sexual behavior was reported. Error bars are  $\pm$  SEM.

compare Table 3). Likewise, neither bleeding nor premenstrual timing significantly predicted the sexual desire variable, and addition of these variables to the models depicted in Table 2 had minimal effects on the coefficients for the hormone variables.

#### *Between-cycle and between-women analyses*

For the sexual contact variable, in a mixed logistic model testing the effects of all three hormones, cycle mean progesterone was a negative predictor of the odds of sex ( $\gamma = -1.01$ ,  $p = 0.047$ , Exp  $b = 0.36$ ), meaning that, within-women, change in average progesterone from cycle 1 to cycle 2 was negatively associated with change in the mean frequency of sex across the two cycles. A separate model testing the effects of subject mean hormone concentrations across the full study revealed no significant effects (all  $ps > 0.15$ ); this means that women who had sex more frequently did not differ in average hormone concentrations from women who had sex less frequently. Parallel models revealed no significant between-cycle or between-women effects of mean hormone concentrations for either woman-initiated sex or masturbation.

## Discussion

### *Sexual desire*

Although many studies had implicated a role for ovarian hormones in the regulation of women's sexual motivation via cycle phase shifts in desire (for a review, see Wallen, 2001), past attempts to document hormonal predictors of within-cycle shifts in libido had produced null results (e.g., Dennerstein et al., 1994; Morris et al., 1987; Persky et al., 1978a,b; Van Goozen et al., 1997). Here, with a much larger sample size and the use of more powerful mixed regression techniques, we identified two hormone variables with opposite effects: estradiol measured two days earlier positively predicted within-cycle fluctuations in sexual desire, as predicted, whereas progesterone was a consistent negative predictor across the current day, one day lag, and two day lag regression models. These effects are consistent with patterns demonstrated in nonhuman primates, as both correlational (e.g., Wallen et al., 1984) and experimental (e.g., Kendrick and Dixon, 1985; Zehr et al., 1998) studies support excitatory and inhibitory effects of estradiol and progesterone, respectively, on measures of female sexual motivation.

Our results also demonstrated higher subjective desire inside the estimated fertile window than at other times in the cycle. Although a number of previous studies had likewise demonstrated such effects, the extant literature was not entirely consistent on this point, as some studies had failed to report mid-cycle peaks (for a review, see Regan, 1996). Only a few of the studies on this topic had, like the current study, used hormone assays (either luteinizing hormone (LH) tests or frequent ovarian hormone sampling) to confirm ovulatory timing, however, and results from those studies point more consistently toward peri-ovulatory peaks in measures of sexual motivation (Bullivant et al., 2004; Dennerstein et al., 1994; Diamond and Wallen, 2011; Hedricks et al., 1994; Wilcox et al., 2004). As such, although a formal meta-analysis of this issue may be warranted, the weight of the current evidence appears to argue strongly for mid-cycle increases in measures of women's sexual motivation.

Positive effects of estradiol and negative effects of progesterone could efficiently explain such mid-cycle peaks in sexual desire given typical patterns of hormone secretion across the menstrual cycle (see Fig. 1). With respect to the drop in sexual desire when moving from ovulation to the luteal phase, we did in fact find strong evidence for statistical mediation by progesterone; because estradiol and testosterone both tend to drop between ovulation and the luteal phase, it was possible that these hormones would mediate the luteal phase drop in desire, but in fact the fertile window effect was just as strong when these hormones were added to the regression model, whereas the fertile window effect dropped out entirely after the addition of progesterone. These patterns argue for progesterone acting as a within-cycle stop signal that produces

luteal phase reductions in sexual desire. With respect to the follicular phase increase in desire when moving from menstruation to the fertile window, though, we were unable to demonstrate substantial hormonal mediation, despite the positive effects of estradiol on desire. This suggests the possibility that other signals of ovulatory timing may play important roles in producing the increases in measures of sexual motivation that are often found just before ovulation (see Fig. 2; Bullivant et al., 2004; Wilcox et al., 2004). Luteinizing Hormone Releasing Hormone (LHRH) and LH are signals associated with impending ovulation, and LHRH in particular has been experimentally linked to higher sexual motivation in nonhuman species (e.g., Barnett et al., 2006; Mauk et al., 1980); likewise, some evidence in humans supports higher oxytocin near mid-cycle, as well positive associations between oxytocin and measures of sexual function (e.g., Salonia et al., 2005). Empirical tests of whether these or other signals may help mediate the ovulatory increase in sexual motivation may have important clinical implications for the possible treatment of hypoactive sexual desire.

Peri-ovulatory increases in sexual motivation may have various biological functions. Promotion of conception is obvious, but chronically high sexual motivation could achieve the same thing, so that the real question here is why motivation drops at other times of the cycle. Sexual behavior has likely entailed fitness costs over the course of evolution—from risk of sexually transmitted infection to opportunity costs in terms of alternative behaviors—and thus the benefit-cost ratio of sexuality may have been greater on average when conception was possible than at other times of the cycle. Fessler (2003) has argued that the competing attentional demands of mating and feeding tend to be resolved in favor of mating during the late follicular phase, and, in general, the progesterone-mediated drop in sexual desire seen in the luteal phase of the present sample (see Fig. 2) could reflect the operation of mechanisms that increase the relative motivation for non-mating tasks during infertile regions of the cycle.

A similar argument for motivational re-prioritization could apply to longer time-scales, and led us to hypothesize between-cycle correlations between estradiol and sexual motivation. Women in human ancestral environments likely often experienced multi-year stretches of suppressed fertility and low ovarian hormones associated with events like lactation and food shortage, and only rarely experienced fertile cycles with higher estradiol (see Ellison, 2001; Lancaster and Kaplan, 2009; Strassmann, 1997); suppression of sexual motivation during these infertile periods could have promoted greater allocation of attention and motivation to more pressing tasks such as maternal care or foraging, with rising estradiol associated with the resumption of fertile cycles then causing the up-regulation of sexual motivation (see Roney, 2009; Roney and Simmons, 2008). Our current data failed to confirm a within-women, between-cycle association between estradiol and sexual desire, however, and the direction of the relationship was actually negative. Restricted variance in estradiol concentrations and the desire variable between the two cycles within the same women likely limited our ability to detect any such effects. Consistent with our hypothesis, though, studies that have followed women longitudinally through the menopausal transition have in fact reported within-women, between-cycle correlations between estradiol and measures of sexual motivation (Dennerstein et al., 2005; Freeman et al., 2007; McCoy, 1990). Demonstration of similar within-women, between-cycle effects in premenopausal women may require following the same women across cycles with larger differences in hormone concentrations than those observed in the present study.

Our data also produced null results with respect to between-women associations between mean hormone concentrations and mean sexual desire, although the power of our design was fairly modest at the between-women level of analysis. The zero-order correlation between subject mean estradiol and mean sexual desire was  $r = 0.23$ , but approximately 75 subjects would be necessary to meet conventional levels of statistical significance for this effect size, as compared to the 43 women in the current design.

Finally, weekend timing was a consistent within-cycle predictor of women's self-reported sexual desire. This effect was independent of the effects of hormone concentrations, which suggests that desire may respond independently to both endogenous fluctuations in hormone concentrations and to external social stimuli that are likely associated with weekend timing in an undergraduate population.

### Sexual behavior

Only a subset of the women in our sample were sexually active, which may have limited our ability to detect hormonal predictors of sexual behavior. Although effects were less consistent than for sexual desire, the within-cycle patterns were similar: positive effects for estradiol, a negative trend for progesterone, and null effects for testosterone. The only effect to reach significance was the association between current day estradiol and the probability of sexual contact: within-cycles, women were more likely to have sex on high estradiol days than on low estradiol days. Effects of current day estradiol on woman-initiated sex and masturbation were positive but marginally significant, and current day progesterone had a marginally significant negative effect on the odds of woman-initiated sex. The effects of weekend timing on sexual behavior were very strong, with weekend days associated with a doubling or tripling of the odds ratios for sexual contact in the within-cycle models (see Table 3). The temporal constraints associated with class schedules and partner availability may have inflated the effects of weekend timing (and obscured the effects of hormonal predictors) in this sample relative to women who cohabit with their partners. Thus, although the overall pattern of results suggests that the positive effects of estradiol and negative effects of progesterone in the within-cycle prediction of sexual desire may also extend to the prediction of sexual behavior, the evidence here is far from definitive and future research that selectively targets women within sexual relationships may facilitate the acquisition of clearer evidence on this issue.

All of the significant or trend-level effects for the behavior variables pertained to current day hormone measures, whereas the strongest effects for sexual desire were found at a two-day lag (see Table 2). The reasons for this pattern are unclear. Genomic effects of hormones may produce synaptic changes at time lags, but hormones like estradiol can also act at shorter time-scales via non-genomic mechanisms (e.g., Stefano et al., 2000); as such, different outcomes could be differentially associated with alternative mechanisms of hormone action. A combination of time-lagged and current day hormone concentrations could provide the strongest prediction of sexual variables if processes of receptor induction need to be combined with current receptor occupation to produce phenotypic outcomes. We were unable to test this possibility in the present study due to missing data associated with days without assays, but such tests represent an interesting direction for future research.

Within-women, between-cycle and between-women effects of hormones on sexual behavior were generally absent, save for a negative effect of cycle mean progesterone on the mean frequency of sex across the two cycles within the same women. This effect was not predicted, but if reliable would suggest that the within-cycle inhibitory effects of progesterone may extend between-cycles, as well. The null results at the between-cycle and between-women levels of analysis for sexual behavior are subject to the same caveats regarding restricted hormone variance and modest power as were explained above for the sexual desire variable.

### Null effects of testosterone

We found no significant effects of testosterone on any variable at any time-scale. This is potentially noteworthy given evidence that exogenous testosterone treatment can improve measures of sexual motivation in menopausal women (e.g., Braunstein et al., 2005; Davis et al., 2008; Floter et al., 2002; Sherwin et al., 1985), and given the common belief

that androgens are the primary regulators of libido in women. Similar null effects for testosterone have been found for correlates of sexual behavior in naturally cycling, group-living rhesus macaques (Wallen et al., 1984). Exogenous testosterone may therefore have pharmacological effects on sexual motivation despite the fact that endogenous testosterone does not play an important role in the regulation of libido in natural menstrual cycles. If sexual motivation in women were regulated by androgens via the androgen receptor, one would expect positive correlations between desire and free testosterone concentrations in natural menstrual cycles since estradiol could not act through this receptor. Exogenous testosterone, on the other hand, could act indirectly via estrogen receptors either by conversion to estradiol (via aromatase) or by the regulation of binding proteins in such a way as to increase the bioavailable concentrations of estradiol (see Wallen, 2001). The absence of testosterone effects in natural cycles thus argues against substantial regulation of libido by androgen receptors in women (normal libido in androgen insensitivity syndrome women suggests the same; see Wisniewski et al., 2000), though more direct empirical evidence regarding receptor involvement is clearly needed.

### Conclusion

The present study replicated peri-ovulatory peaks in women's subjective sexual desire, but also identified hormonal predictors of within-cycle fluctuations in desire. Progesterone had a consistent negative effect on desire across time-lags, and appears to act as an inhibitory signal for sexual motivation; estradiol had a positive effect on desire at a two-day lag. Effects for sexual behavior were less clear, but also implicated positive effects of estradiol and negative effects for progesterone. Significant limitations of the present study include its use of an undergraduate population that may differ in important ways both hormonally and behaviorally compared to older women, and our inability to assay samples from every day of the study due to financial constraints, which precluded testing multiple time lags in the same regression models. Collection of complete hormone data from more representative, community-based samples of women thus represents an important direction for future research.

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### Appendix A

The formal regression equations for the mixed models, using the current day model depicted in Table 2 (main text) as an example, were as follows:

Level-1 model:

$$Y_{ijk} = \pi_{0jk} + \pi_{1jk} * (\text{weekend}) + \pi_{2jk} * (\text{estradiol}) + \pi_{3jk} * (\text{progesterone}) + \pi_{4jk} * (\text{testosterone}) + \epsilon_{ijk}$$

Where

$Y_{ijk}$  = Sexual desire rating on day  $i$  in cycle  $j$  for person  $k$

$\pi_{0jk}$  = Intercept for sexual desire within cycle  $j$  for person  $k$

$\pi_{1jk} \dots \pi_{4jk}$  = Regression slopes for predictor variables in cycle  $j$  for person  $k$

$\epsilon_{ijk}$  = Error term (residual) associated with day  $i$  in cycle  $j$  for person  $k$

Level-2 model:

$$\pi_{0jk} = \beta_{0k} + \Gamma_{0jk}$$

$$\pi_{1jk} = \beta_{10k}$$

$$\pi_{2jk} = \beta_{20k}$$

$$\pi_{3jk} = \beta_{30k}$$

$$\pi_{4jk} = \beta_{40k}$$

Where

$\beta_{0k}$  = Intercept for sexual desire for person  $k$

$\Gamma_{0jk}$  = Error term for cycle mean sexual desire in cycle  $j$  for person  $k$

$\beta_{10k}$  ...  $\beta_{40k}$  = Average regression slopes for predictor variables for person  $k$

Level-3 model:

$$\beta_{0k} = \gamma_{000} + \mu_{00k}$$

$$\beta_{10k} = \gamma_{100}$$

$$\beta_{20k} = \gamma_{200}$$

$$\beta_{30k} = \gamma_{300}$$

$$\beta_{40k} = \gamma_{400}$$

Where

$\gamma_{000}$  = Grand mean for sexual desire

$\mu_{00k}$  = Error term for person  $k$  mean sexual desire

$\gamma_{100}$  ...  $\gamma_{400}$  = Average regression slopes for predictor variables computed across all cycles and subjects using maximum likelihood estimation

Mixed model:

$$Y_{ijk} = \gamma_{000} + \mu_{00k} + \Gamma_{0jk} + \gamma_{100} * (\text{weekend}) + \gamma_{200} *$$

$$(\text{estradiol}) + \gamma_{300} * (\text{progesterone}) + \gamma_{400} * (\text{testosterone}) + \epsilon_{ijk}$$

The within-cycle models included only Level-1 predictors (see above) since within-women, between-cycle effects could only be tested for women with two cycles of hormone data, such that addition of Level-2 predictors would have led to information loss at Level-1. We then constructed separate models with only Level-2 or Level-3 predictors to test within-women, between-cycle and between-women effects. Within-women, between-cycle effects were tested by entering cycle-centered mean hormone variables (e.g., cycle mean estradiol minus subject mean estradiol) as predictors of  $\pi_{0jk}$  in the Level-2 model. Between-women effects were tested by entering subject mean hormone concentrations as predictors of  $\beta_{0k}$  in the Level-3 model. By entering predictors at only one level, the higher level models were able to include all days for which survey responses were available (e.g., subject mean estradiol was tested for prediction of subject mean desire computed across all survey days instead of only those days with hormone assays), which maximized use of available information; however, the null effects of higher level variables reported in the text were still found if Level-2 and Level-3 predictors were added to models that included the Level-1 predictors and thus restricted analyses to those days with hormone assays.

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