Moods in Everyday Situations:

Effects of Menstrual Cycle, Work, and Stress Hormones

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Abstract

Objective: This study examined women's mood responsiveness on work and off days during different phases of the menstrual cycle. *Methods*: Self reports of negative, positive, and energy dimensions of mood were obtained throughout the day on two work and two off days during the luteal and follicular phases of the menstrual cycle in 203 women nurses. Individual differences in daytime and nighttime epinephrine, norepinephrine, and cortisol were assessed. *Results*: High daytime norepinephrine, epinephrine, and cortisol levels were associated with higher ratings of stress and tired, and with lower ratings of happy. Phase of the menstrual cycle and the day factor (work day, off day) were also associated with mood differences, and the direction of the effects depended on hormone levels and hormone sampling period. *Conclusion*: The experience of moods is affected by arousal-related interaction of hormone levels with phase of the menstrual cycle and occupational stress.

Key words: Arousal, Epinephrine, Norepinephrine, Cortisol, Mood, Menstrual cycle

Introduction

Reviews of psychological processes associated with the menstrual cycle indicate that depression, irritability, insomnia, fatigue, and anxiety are most frequently linked to the luteal phase. Several studies reported higher ratings of negative moods in the luteal than in the follicular phase [1, 2], but others concluded that affective fluctuations across the menstrual cycle are uncommon [3, 4]. In a previous study [5], we showed that phase of the menstrual cycle was associated with differences in the ratings of anxious, stressed, tired, happy, and sad, depending on the day (work, off work) and individual differences in affective traits. We proposed that the follicular and luteal phases *per se* do not determine positive or negative moods, but rather serve to dampen or magnify emotional arousability depending on other arousal-related factors such as environmental stress. This accords with studies proposing that a higher level of estrogens in the luteal compared to follicular phase produces more general arousal via central effects (e.g., corticotropin releasing factor) on the hypothalamic–pituitary–adrenal (HPA) and sympatho-adrenomedullary (SAM) systems [6, 7].

The most keenly debated issue concerns the apparent equivocal nature of the relationship between HPA or SAM stress hormones (epinephrine, norepinephrine, and cortisol) and self-reported distress (anxiety, depression, and stress). Although a substantial literature has identified increased stress hormone levels in populations reporting high levels of distress [8, 9, 10] and in clinically depressed patients [11, 12]; other investigations have not shown these associations [13, 14, 15] or have reported effects in the opposite direction [16, 17]. Inconsistencies in findings may be a function of different methods of sampling hormone levels [18] or differences in the kinds of acute and chronic stressful events studied [19]. With morning samples, the relationship between stress hormones and affective states was positive [20, 21, 22], whereas daytime or evening samples showed a negative relationship to distress onset (anxious or depressed moods) and poor performance [17, 23], at least for cortisol and norepinephrine. Distress may affect not only absolute hormone levels but also the diurnal profile of hormone release [18, 19]. In contrast to acute stress, in prolonged occupational stress the circadian

stress hormone rhythm decreases below minimum levels [24]. Occupational stress increases physiological arousal (e.g., SAM hormone levels) during work days in contrast to off days [7].

Although Eysenck's arousal/activation theory is not associated directly with positive and negative emotional states apart from the notion that there are optimal and suboptimal levels of cortical arousal for hedonic tone (pleasure vs. displeasure, [25]), this framework suggests that valence differences in moods may be unobservable in the absence of a difference in physiological arousal (see, e.g., [26]). Moreover, a pattern of arousal factors should be considered for proper assessment of more enduring states of mood-related arousal (see, e.g., [27]). In accordance with arousal/activation theory, the prior studies suggest that individuals who are in a midarousal state will show less disturbance in their behavior or emotional state [28, 29, 30, 31], whereas either downward or upward deviation from optimal arousal level will be associated with greater disturbance. Thus, a hyperarousal condition (e.g., complex of higher stress hormone level, higher arousal menstrual phase, greater environmental/social stress) should determine negative mood states, and a hypoarousal condition (e.g., complex of low stress hormone level, lower arousal menstrual phase, lower stress) should also be related to negative mood states, whereas a midarousal condition should be related to positive mood states.

It follows that stress hormone level should affect mood valence in different ways depending on menstrual cycle phase and stress. A high stress hormone level coupled with one or several other arousal-related factors (e.g., with higher estradiol during the luteal phase and/or stress) should determine high negative mood states, and a low stress hormone level coupled with lower estradiol during the follicular phase and/or lower stress should also determine high negative mood states. In these cases, a change of stress hormone level to a lower value in the former case and to a higher level in the latter case should convert negative to more positive mood.

We examined self reports of moods throughout the day on both work and off days in two phases of the menstrual cycle in a large sample of nurses. Based on previous research, we assumed that the work day involves greater stress than a nonwork or off day. The data were obtained in a study of psychosocial factors affecting ambulatory blood pressure and hormones (see Goldstein et al. [7],

Goldstein and Shapiro [32], Shapiro et al. [33], and Davydov et al. [5]). The moods were rated by the nurses each time their blood pressure and heart rate were recorded throughout the day. In this paper, the relation between moods and endocrine measures is examined as a function of menstrual cycle phase (follicular, luteal) and day (work day, off day). We predicted that women in a stressful occupation would exhibit fluctuations in moods as a function of hormone levels, menstrual phase, and work/nonwork day. We focused on moods that from the literature seem relevant to women's biological and behavioral conditions. In view of the findings that stress-related hormonal activation can not only accompany but can also follow mood changes [16, 19], samples of stress hormones (epinephrine, norepinephrine, cortisol) were obtained both at the end of the day and at the end of the nighttime period following the day in which the mood ratings were obtained.

Method

Subjects

The subjects were 203 healthy registered nurses with at least one year of experience in nursing, premenopausal women between the ages of 24 and 50 (37.7 (6.6), mean (SD)) employed in hospitals and clinics. Subjects worked on daytime 8-hour (48%), 12-hour (50%), or 10-hour shifts (2%). Exclusions were health problems, use of medications or oral contraceptives, severe obesity (BMI >30kg/m^2), pregnancy or childbirth within the last 12 months, or irregular menstrual cycle. The sample included 58% White, 14% African, 15% Latino, and 13% Asian Americans.

Design

Subjects were studied during two phases of their menstrual cycle. For the follicular phase, subjects were scheduled on days 4 to 8 after the beginning of menstruation; for the luteal phase, subjects were scheduled 5 to 10 days after the surge in luteinizing hormone, as determined by the Clearplan home ovulation testing kit (Fisons Consumer Health, Sydney, Australia). This kit uses monoclonal antibody technology to detect the amount of luteinizing hormone normally occurring 24 to 36 hours before ovulation [34]. Days were adjusted for women with cycles longer or shorter than 28 days. To confirm

the occurrence of ovulation in the postovulatory phase, plasma progesterone levels were measured during the luteal phase.

Subjects participated in an initial orientation session followed by 4 24-hour ambulatory recording days during which blood pressure and heart rate were recorded every 30 minutes on a variable schedule. The recording was done on 2 work days and 2 off work days over a period of a few months. Half the subjects began the 4-day sequence in the follicular phase and half in the luteal phase, followed by the other study days in succession. Within phase, day (work, off) was counterbalanced. Recordings within cycle were done at least one day apart. Complete data were obtained on 171 nurses, and 32 subjects completed at least one work day and one off day in one or the other phase.

Moods

Subjects filled out a paper-and-pencil diary each time they felt the blood pressure cuff inflate. They completed the diary on 90% of the scheduled occasions. On the average, 46 sets of diary entries per day per subject were available for analysis. Subjects used a 5-point numerical scale from "none" to "extreme amount" to rate the following moods: stressed, happy, frustrated, alert, angry, sad, conflicted, tired, anxious, in control. The ratings tended to be clustered in three dimensions reflecting negative, positive, and energy components of mood (see [33]). As the analyses showed consistent patterns for most of the moods, to simplify this presentation one mood was selected for analysis from each dimension: stressed, happy, and tired. These mood terms had the widest dispersion of ratings.

Biochemical Assays

For each of the four sessions, urine was collected over a 24-hour period and stored in two separate bottles for the waking (daytime and evening) period and the period at night during sleep at the end of the day. Nighttime samples included all urine output collected during the night. Complete details on the biochemical assays and methods can be found elsewhere [7].

In keeping with our previous analytic approach [7], hormones levels were each split at the median into high and low groups. The split was made as close as possible to 50%. Instead of a common value based on the average hormonal level for all sessions of a given subject, we dichotomized each session's hormonal data into high and low daytime (D) and nighttime (N) groups. The variables were as follows: Depi, Dnor, and Dcor for daytime epinephrine (Epi), norepinephrine (Nor), and cortisol (Cor) and Nepi, Nnor, and Ncor for nighttime epinephrine, norepinephrine, and cortisol.

Data Analysis

The data consist of longitudinal self-ratings of moods on four days. As exemplified in recent papers [35], random effects regression models are appropriate for the longitudinal data obtained in ambulatory studies. The models consider both within- and between-subject variability, and allow for random and fixed effects as well as a variable number of observations per subject and missing data. PROC MIXED (SAS Institute) was the program used for general linear mixed modeling. Modeling each subject as a random effect accommodates interindividual variation in mood-phase-day-hormone relationships, and allows a standardized evaluation of these relationships. Each subject acts as her own control over time. The repeated measures of each one of the six moods related to Day (off, work) and Phase (follicular, luteal) independently of other factors were reported in the previous paper (see [5]). In each model, we added the six dichotomized hormonal groupings (levels) one at a time. Phase, day, and hormone level were treated as class variables in the analyses. For significant interactions (p values $< .05$), PROC MIXED compared cell means by t test. Inasmuch as we tested specific hypothesis in terms of the direction of effects and as the analyses of the other moods not presented here showed consistent significant patterns, statistical significance for t tests was attributed to p values $<.10$ for predicted directions. For all PROC MIXED F tests the df are 1/34000.

Results

Means and standard errors of mood scores for main and interaction effects are presented in Tables 1 and 2. Table 2 includes an interpretation of the interactive effects in terms of overall arousal.

Main Effects

Main Phase and Day effects were reported in the previous paper (see [5]). Significant main effects for Depi were obtained for stress ($F = 28.20$, $p<.0001$) and tired ($F = 4.76$, $p<.05$). Ratings of stress and tired were lower in the low Depi level compared to the high Depi level. Significant main effects for Dnor were obtained for stress ($F = 7.64$, $p<.01$) and happy ($F = 4.45$, $p<.05$). Ratings of stress were lower and ratings of happy were higher for low Dnor compared to high Dnor. Significant main effects for Dcor were obtained for stress ($F = 13.15$, $p<.0005$). Ratings of stress were lower for low Dcor compared to high Dcor. No main effects were obtained for nighttime hormone samples (Nepi, Nnor, Ncor) for these mood ratings.

Interaction Effects

Interaction Phase X Day effects were reported in the previous paper (see [5]). No interaction Epi X Phase X Day effects were obtained for the reported mood ratings.

Significant interactions were found between Nnor, Phase, and Day for happy ($F = 9.81$, $p<.005$). Higher ratings of happy were found during the luteal phase compared to the follicular phase for high Nnor (t's $p=.032$), and the effect was opposite for low Nnor (t's $p=.081$). Higher ratings of happy were found for low Nnor compared to high Nnor (t's $p=.002$), but only for the follicular phase. The differences were significant only during the off day.

Significant interactions were found between Nnor and Phase for tired ($F = 14.49$, $p<.0001$). Higher ratings of tired were found during the luteal phase compared to the follicular phase for high Nnor (t's $p=.041$), and the effect was opposite for low Nnor (t's $p=.001$). Higher ratings of tired were found for low Nnor compared to high Nnor (t's $p=.044$) during the follicular phase, and the effect was opposite during the luteal phase (t's $p=.003$).

Significant interactions were found between Dcor, Phase, and Day for happy ($F = 5.66$, $p<.05$). Higher ratings of happy were found during the luteal phase compared to the follicular phase for low Dcor (t's $p=.068$), and the effect was opposite for high Dcor (t's $p=.064$). Higher ratings of happy

were found for low Dcor compared to high Dcor (t's p=.026) during the luteal phase. However, the differences were significant only during the work day.

Significant interactions were found between Dcor and Day for tired (F = 10.58, p<.001). Higher ratings of tired were found during the work day compared to the off day for high Dcor level (t's p=.000). Higher ratings of tired were found for high Dcor compared to low Dcor (t's p=.001), but only on the work day.

Significant interactions were found between Ncor and Phase for stress (F = 6.01, p<.05). Higher ratings of stress were found during the follicular phase compared to the luteal phase for high Ncor (t's p=.007). Higher ratings of stress were found for high Ncor compared to low Ncor (t's p=.014) during the follicular phase.

Significant interactions were found between Ncor and Phase for happy (F = 5.30, p<.05). Higher ratings of happy were found during the luteal phase compared to the follicular phase for high Ncor level (t's p=.073). Higher ratings of happy were found for high Ncor compared to low Ncor (t's p=.043) during the luteal phase.

Discussion

Although the observed differences in mood reports were relatively small in magnitude, they yielded consistent significant effects related to level of stress hormones, type of day (work, off) and menstrual cycle phase (follicular, luteal) in this sample of healthy women. Note that the mean differences are based on dichotomized hormone measures. The study findings supported the hypothesis that negative or distressful mood states are related to concurrent (daytime) as well as following (nighttime) response levels of two arousal- or stress-related HPA and SAM systems. Independently of phase and day, high daytime cortisol level was related to higher ratings of stress, high daytime epinephrine was also related to higher ratings of stress as well as tired, and high daytime norepinephrine was related to higher ratings of stress as well as lower ratings of happy. In contrast, compared to daytime hormone measures, the relation between nighttime hormone values and the moods stress and happy was in the opposite direction and depended on phase of the menstrual cycle and/or day.

Other findings confirmed the hypothesis that the follicular and luteal phases *per se* do not determine positive or negative moods, but rather serve to dampen or magnify emotional arousability depending on other factors. Relatively high or low stress hormone levels were related to both high and low levels of stress depending on the general arousal level as determined by cycle phase and day. This accords with the proposal of Morgan and Pfaff [6] that a higher level of estrogens produces more general arousal ("arousal-up" estrogen effect) via effects on corticotropin releasing factor, which may be expressed behaviorally as increased reactivity (e.g., anxiety/fear) in a potentially stressful environment. However, the interactive effects of phase and hormone levels on some moods (e.g., happy and stress) showed results in the opposite direction for nighttime samples of stress hormones as compared to daytime samples (see Table 2). The same consistent daytime/nighttime contrast was found for other negative moods (anxiety and sad), not presented in this paper.

One explanation of this contradiction may be the effect of stress on diurnal variations of stress hormones usually observed in chronic stress [24]. These variations (early morning maximum, declining levels throughout the day, a quiescent period of minimal secretory activity around midnight, and an abrupt elevation during late sleep) are well-known. However, negative daily events and stress have been found to affect diurnal patterns of stress hormone levels as shown by a drop of values below 'normal' following an increase of values above 'normal' [18, 19]. The opposite interactive effects on moods of daytime vs. nighttime stress hormones may be explained by an enhanced inhibitory or negative feedback mechanism in higher distress conditions [19, 36]. Thus, we assumed that this nighttime rebound effect would be greater for subjects under higher daytime distress in contrast to subjects in lower distress as measured by average levels of daytime moods. However, for some moods (e.g., tired), the relations were in the same direction for both daytime and nighttime samples, which could mean that the arousal in these states was maintained from daytime to nighttime (see Table 2). It is possible that the arousal level of these mood conditions reduces or blocks negative feedback mechanisms for some stress hormones [19] as may occur in some depressed patients [37]. In future studies analyses need to be conducted to confirm that the level of reported distress or negative mood

(low happy and high stress moods) can be positively related to the magnitude of the difference between daytime and nighttime stress hormone levels.

Although all three daytime hormone measures showed expected main effects for mood, no main effects were obtained for the nighttime measures. For the latter measures, only interactive effects were found involving cortisol and norepinephrine but not epinephrine. However, several main nighttime hormone effects and interactive effects involving epinephrine were found for other moods not presented in this paper, in particular the negative moods anxiety, sad, and anger.

Following the findings of arousal-related research [28, 29, 30, 31], our study confirmed that an increase in arousal beyond the optimal level due to the coupling of several high arousal factors (e.g., high SAM or HPA daytime hormones in the luteal phase or nighttime rebound mirror of low SAM and HPA hormones in the luteal phase) was associated with an increase in negative moods. However, an increase in arousal helped improve mood in subjects in relatively low arousal conditions (follicular phase or off day) by shifting their level of arousal due to high SAM or HPA daytime hormone levels increasing to an optimal level. On the other hand, a decrease in arousal below the optimal level due to coupling of several low arousal factors (e.g., low SAM or HPA daytime hormones in the follicular phase) also tended to increase distress or negative mood. Therefore, the results support our main proposal and suggest that to the extent that mood differences exist between hyperarousal and hypoarousal conditions, we should expect a midarousal state to be associated with positive mood. Balanced mild arousal compensated for high or low activation related to cycle phase or stress hormones was associated with positive mood. Hormone/day interactions showed effects similar to those found for hormone/phase interactions. Different levels of stress associated with work or nonwork days could dampen (off day) or magnify (work day) arousal effects of phase and hormones.

The findings in this study help explain inconsistencies in theliterature showing that subjects reporting increased distress or clinically depressed patients had both increased and decreased stress hormone levels and reactivity [8, 9, 10, 11, 12, 16, 17, 38, 39, 40]. The results suggests that both high and low stress hormone levels can be associated with negative moods in the same subject depending on

hormone sampling period in menstrual and diurnal cycles. A similar homeostatic arousal-related influence of CO_2 partial pressure on negative (anxious/fear) mood has been reported [41]. Thus, the current findings support the view that positive emotional processes normally function within a mild arousal level, at a homeostatic midpoint. Both hyperarousal and hypoarousal may lead to dysfunction and distress, as shown in increased negative moods or an aberration in positive moods as an alarm or motivational signal [42].

The findings seem to contradict experimental studies of situational (acute) affective responses and the two-dimension valence/arousal hypothesis (see, e.g., [43]), which showed that the same high autonomic (e.g., SAM system) arousal accompanies responses to both positive and negative emotional stimuli. In these studies a single measure of general arousal has been employed. However, some of their findings demonstrated a difference in autonomic patterning of reactivity. High sympathetic arousal specific to both positive and negative affects has been shown to be coupled with higher parasympathetic regulation of cardiac reactivity as a possible compensation for the higher sympathetic arousal occurring in negative affective compared to positive affective states (see, e.g., [43]). That suggests that a single measure of general arousal balance is insufficient. Moreover, another study showed that negative pictures elicited increases in norepinephrine, cortisol, and adrenocorticotrophic hormone, pleasant pictures had no effect on the stress hormones, but "neutral" (i.e. boring) stimuli decreased stress hormone levels [44]. These results seem to support and expand the above-stated homeostatic hypothesis of mood and emotion regulation to affective responses.

Thus, in contrast to males, in women, vulnerability to cardiovascular diseases and affective disorders may be related to cyclic activity of reproductive hormones that affect mood fluctuations. It is reasonable to propose that in women the activity of stress-related hormones compensates for the variability of arousal level determined by sex hormones via a specific feedback mechanism or via coupling by a common functional system. Changes in mood in some women during the menstrual cycle may be a result of disruption in this process.

In conclusion, by using real-time assessments of mood we have been able to determine that the experience of certain moods is associated with daytime and nighttime HPA and SAM hormonal levels and their interaction with phase of the menstrual cycle and environmental stress. This interplay of factors suggests the need to develop further and refine arousal-related models of the regulation of mood and bodily systems and of risk for disease.

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Table I. Significant main effects for daytime hormone levels. (Epi = epinephrine, Nor = norepinephrine, Cor = cortisol).

Hormone level		
High	Low	Mood (Mean (SE))
Epi		High stress (1.62 (0.03))
	Epi	Low stress (1.52 (0.03))
Nor		High stress (1.59 (0.03))
	Nor	Low stress (1.54 (0.03))
Cor		High stress (1.60 (0.03))
	Cor	Low stress (1.53 (0.03))
Epi		High tired (2.01 (0.04))
	Epi	Low tired (1.94 (0.04))
Nor		Low happy (2.99 (0.06))
	Nor	High happy (3.03 (0.06))

Table II. Significant interactive effects on mood of High vs. Low hormone level, menstrual cycle Phase, and Day. (L = luteal phase, F = follicular phase, W = work day, NW = off day, Nor = norepinephrine, Cor = cortisol)

Hormone level						Relative mood level	Proposed general
Daytime		Nighttime					
High	Low	High	Low	Phase	Day	(Mean (SE))	arousal state
		Cor		L		High happy (3.04 (.06))	Midarousal
			Cor	L		Low happy (2.98 (.06))	Hyperarousal
		Cor		F		Low happy (3.00 (.06))	Hypoarousal
	Cor			L	W	High happy (2.98 (.07))	Midarousal
Cor				L	W	Low happy (2.90 (.07))	Hyperarousal
	Cor			F	W	Low happy (2.92 (.07))	Hypoarousal
Cor				F	W	High happy (2.96 (.07))	Midarousal
			Nor	F	NW	High happy (3.13 (.07))	Midarousal
		Nor		F	NW	Low happy (3.02 (.07))	Hypoarousal
		Nor		L	NW	High happy (3.09 (.07))	Midarousal
			Nor	L	NW	Low happy (3.07 (.07))	Hyperarousal
		Cor		L		Low stress (1.55 (.03))	Midarousal
			Cor	F		Low stress (1.55 (.03))	Midarousal
		Cor		F		High stress (1.61 (.03))	Hypoarousal
Cor					W	High tired (2.07 (.04))	Hyperarousal
	Cor				W	Low tired (1.94 (.04))	Midarousal
Cor					NW	Low tired (1.92 (.04))	Midarousal
		Nor		F		Low tired (1.94 (.04))	Midarousal
			Nor	F		High tired (2.02 (.04))	Hypoarousal
		Nor		L		High tired (2.01 (.04))	Hyperarousal
			Nor	L		Low tired (1.90 (.05))	Midarousal