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Abstract

Objective: This study examined women's mood responsiveness associated with patterns of stress hormone levels in everyday situations. *Methods*: Self reports of negative, positive, and energy dimensions of mood were obtained in 203 nurses throughout the day on a work day and an off day during the luteal and follicular phases of the menstrual cycle. Individual differences in daytime norepinephrine and cortisol were assessed. *Results*: Patterns of norepinephrine and cortisol level were associated with ratings of the moods tired, sad, and happy. Phase of the menstrual cycle and the day factor (work day, off day) modified the association of mood ratings and stress hormone patterns. *Conclusion*: The experience of negative mood is associated with both hypoarousal and hyperarousal conditions. A homeostatic arousal-related concept of mood regulation is discussed.

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

1. Introduction

Some authors distinguish stress hormones (norepinephrine, epinephrine, and cortisol) relative to the dimensions of arousal and emotional valence, and others have emphasized their similar response to stress. Frankenhaeuser [1] proposed that catecholamines, particularly epinephrine, are indicators of arousal and are unrelated to positive or negative affect, and that cortisol generally increases during negative affect. She referred to increased norepinephrine and epinephrine with no increase in cortisol as effort without distress. When elevations in catecholamines are accompanied by increases in cortisol, it was considered to be a sign of negative emotion or distress.

However, different stress-related behaviors and tasks have been shown to elicit significant increases in plasma levels of epinephrine and norepinephrine [2 - 5]. In some studies, brief psychological stressors have elicited hypothalamic–pituitary–adrenal (HPA) activity manifested in elevated levels of adrenocorticotropic hormone [3] or cortisol [6]. Epinephrine can increase secretion of corticosteroids [7], and cortisol has been shown to inhibit the reuptake of catecholamines, thereby potentiating the effect of norepinephrine on heart rate and contractility [8, 9]. Catecholamine as well as glucocorticoid secretion are essential to the mobilization and regulation of bodily resources and, via brain transmitter systems (e.g., catecholaminergic, dopaminergic, serotinergic, and gabaergic activity [10]), increase excitability and synaptic transmission [11] in the hypothalamus, the locus coeruleus, the amygdala, and the prefrontal cortex [12 - 17], producing arousal effects [18] and affecting mood [19, 20]. Although a substantial literature has identified increased stress hormone levels in populations reporting high levels of distress [21 - 24] or in clinically depressed patients [25, 26], other investigations have not shown this association [27 - 29] or have reported opposite effects [30, 31]. The association of higher symptoms of

distress with elevated levels of epinephrine, norepinephrine, and cortisol at one month after posttraumatic stress disorder was evident in men, but not in women [21].

Sex hormones (e.g., estrogens) are other arousal-regulating hormones known to affect a variety of behaviors related to emotions, activity levels, and mood. Experimental findings [32] indicate that a higher level of estrogens is associated with arousal effects, e.g., increased behavioral activity or fear. Human and animal studies suggest that the influence of estrogens on non-reproductive processes is variable in both amplitude and direction; effects may depend on the current state of the organism [33 - 35]. Despite a long history of examining the role of estrogens in non-reproductive behaviors such as activity and affect, the results are ambiguous.

In a previous paper [34], the apparent equivocal nature of the relationship between HPA, sympatho-adrenal-medullar (SAM), and sex hormones in their effect on self-reported distress was interpreted in terms of the impact of stress hormone levels on arousal in relation to menstrual phase, a proxy for estrogen levels, and environmental context. Both hyperarousal and hypoarousal conditions, as determined by stress and sex hormone levels, were associated with negative mood, whereas positive emotions tended to function within a mild arousal level. Although cortisol, norepinephrine, and epinephrine all showed an expected similar interaction with the arousal effects of menstrual phase and day (work, nonwork) on mood, more consistent results were obtained for cortisol than for catecholamines. Differences in the arousal impact of hormones were hypothesized to be the main source of this difference.

Historically, arousal has been a critical concept in neurophysiology and the study of behavior, but it is complicated by definitional ambiguity. One of the main issues is the need to find a common measure or scale of arousal. New experimental studies [35] and our previous findings [33, 34] suggest that moods may provide such a measure. In our studies,

an arousal process has been defined as an energy-consuming process distributed from a local to general (organism) level, which is associated with biological or psychological processes. In the current paper, we have analyzed factors (stress and sex hormones, job stress), which affected general arousal level. A homeostatic arousal-related concept of mood regulation tested in this paper considers the joint impact of norepinephrine, cortisol, menstrual phase, and occupational stress (work day or off-work day) on arousal level. In turn, deviation of general arousal from a homeostatic level affects mood. Although we assumed that HPA and SAM hormones have a different impact on general arousal, this issue was left unresolved in our previous paper [34]. To date, evidence is lacking on the comparison of the arousal impact of HPA and SAM systems on mood as a function of different physiological (e.g., estrogen level) and environmental (e.g., occupational stress) factors. As norepinephrine and cortisol showed more reliable relationships to moods in this sample of subjects [34], this paper focuses on the interactive effects of these hormones.

A common conception about stress hormones (e.g., cortisol) is that acute elevations cause feelings of stress, anxiety, or negative affect. However, numerous case studies have described euphoric effects of open label treatment with cortisol or cortisone (e.g., [36]), and the current literature suggests that acute pharmacologically-induced cortisol elevations have varying effects on mood, often with no effect on affective state or only mild mood elevation (e.g., 37 - 39). The homeostatic hypothesis [34] predicts that a decrease or increase in any arousal factor (e.g., cortisol) improves mood if it shifts general arousal toward a homeostatic level, but a decrease or increase in an arousal factor disturbs mood if it moves general arousal away from a homeostatic level. Individuals who are in a midarousal state will show less disturbance in their emotional state, whereas either downward or upward deviation from an optimal arousal level will be associated with greater disturbance. An optimal level of arousal is determined by the joint impact of

arousal-related factors in which the higher or lower level of one factor is compensated for by the higher or lower level of another arousal factor. Although different arousal-related factors may have different effects on arousal, a hyperarousal condition (e.g., complex of two higher stress hormone levels) should be associated with negative mood states, and a hypoarousal condition (e.g., complex of two lower stress hormone levels) should also be related to negative mood states, whereas a midarousal condition (e.g., complex of both higher and lower stress hormone levels) should be related to positive mood states.

Based on our previous findings [34] we predicted that a combination of high and low levels of different stress hormones in the high arousal luteal phase of the menstrual cycle (a proxy of higher estrogen level) would show a higher arousal effect on mood than the same coupling of hormone levels in the low arousal follicular phase (a proxy of lower estrogen level). That is, the effects of patterns of stress hormones should affect mood valence in different ways depending on phase of the menstrual cycle. Occupational stress should also affect these relationships [33, 34]. In this paper, the experimental data [34] were re-examined to assess the combined effects on moods of two stress-related hormones, one from the HPA axis and one from the SAM system, in different menstrual (follicular and luteal phase) and environmental (on-work/off-work) conditions.

We examined self reports of moods throughout the day on a work day and on an off day in two phases of the menstrual cycle in a large sample of nurses. We assumed that the work day involves greater arousal than the off day in this sample of subjects and defined it as an independent "occupational stress" factor, because in our previous studies [33, 34, 40] it has been related to higher ratings of negative moods and increased activity of the cardiovascular and SAM system. A higher level of estrogens in the luteal compared to follicular phase was expected to produce more general arousal [32, 34, 35]. The data were obtained in a study of psychosocial factors affecting ambulatory blood pressure and

hormones in nurses (see [33, 34, 40 - 42]). The moods were rated by the nurses each time their blood pressure and heart rate were recorded throughout the day by an ambulatory recorder.

2. Methods

2.1 Subjects

The subjects were 203 healthy registered nurses with at least one year of experience in nursing. They were all premenopausal women between the ages of 24 and 50 (37.7 (6.6), mean (SD)). Subjects worked in hospitals and clinics on daytime 8-hour (48%), 12-hour (50%), or 10-hour shifts (2%). Exclusions were acute or chronic illnesses, mental health problems, use of medications or oral contraceptives, obesity (BMI > 30 kg/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. Complete details on the subject selection can be found elsewhere [40, 42].

2.1 Design

Subjects were studied during two phases of their menstrual cycle. For the follicular (F) phase, subjects were scheduled on days 4 to 8 after the beginning of menstruation; for the luteal (L) phase, subjects were scheduled 5 to 10 days after the surge in luteinizing hormone. Phase was 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 [43]. Days were adjusted for women with cycles longer or shorter than 28 days. To confirm the occurrence of ovulation in the postovulatory phase and sex hormone differences between menstrual phases, plasma estrogen and progesterone levels were measured during the F and L phase.

Subjects participated in an initial orientation session followed by four 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 two work days and two off work days over a period of a few months. The interval between recording days was related to the subject's menstrual cycle. Half the subjects began the 4-day sequence in the F phase and half in the L phase, followed by the other study days in succession. Within phase, day (work, off) was counterbalanced. Recordings within each menstrual cycle were done at least one day apart. Complete data were obtained on 171 nurses. Additionally, 32 subjects completed at least one work day and one off day in one or the other phase. Complete details on the design and methods can be found elsewhere [40, 42].

2.2 Moods

Subjects filled out a paper-and-pencil diary each time they felt the blood pressure cuff inflate. Diaries were completed on 90% of the scheduled occasions. On 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. Subjects varied in the extent to which they used all 5 levels of response, some restricting their response to 2 or 3 levels. The Mixed Regression Analysis (see below) accounts for these individual differences. The ratings tended to be clustered in three dimensions reflecting negative, positive, and energy components of mood (see [42]). Previous analyses showed consistent effects within each of these dimensions of mood [33, 34]. To simplify this presentation, the results for one positive mood (happy), one negative mood (sad), and one energy-related mood (tired) are presented.

2.3 Biochemical Assays

For each of the four sessions, urine was collected over a 24-hour period and stored in one

bottle for the waking (daytime and evening) period and one for the period at night during sleep. The daytime samples are considered here. To correct for differences in urinary volume, epinephrine, norepinephrine, and cortisol levels were divided by the concentration of creatinine, resulting in units of measurement in terms of nanograms per milligram of creatinine. These values were log transformed in the statistical analyses. Complete details on the biochemical assays and methods can be found elsewhere [40]. In keeping with our previous analytic approach [34, 40], hormone levels were each split at the median into high and low groups. Although some information related to linear variation of a single hormone may be lost, the median split was advantageous in detecting non-linear relationships between several arousal factors (here, pattern of hormones) and mood variations in paired comparison contrasts [34]. The split was made as close as possible to 50%. Instead of a common value based on the average hormone level over all four days for a given subject, we dichotomized each day's hormone values into high and low subgroups. To simplify this presentation, the two hormones showing the most reliable effects in the previous study [34] were selected for analysis, norepinephrine and cortisol. The variables are labelled Nor and Cor for daytime norepinephrine and cortisol.

2.4 Data Analysis

The data consist of longitudinal self-ratings of each of three mood ratings (happy, sad, tired) on four days. As exemplified in recent papers [44], random effects regression models are appropriate for the longitudinal data obtained in ambulatory blood pressure 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. In each model tested, each mood was the dependent variable. As independent variables, we included Nor and Cor levels (high, low), Day (off, work), and Phase (follicular, luteal). Each Hormone level, Day, and Phase were treated as class variables in the analyses. Analyses of the repeated measures of each one of the moods related to Day and Phase and of each one of the hormones treated separately in interaction with other factors were reported in previous papers (see [33, 34]). Reported here are effects involving the interaction of Nor and Cor.

In the PROC MIXED random regression model, subjects and the successive mood ratings are treated as repeated measures. An autoregressive model (lag = 1) was used to control for the serial correlation of the successive mood ratings. PROC MIXED compared the least square cell means by *t* test using the Tukey-Kramer adjustment for multiple pair-wise comparisons, the most conservative method. Statistical significance was attributed to *p* values < .05 for the predicted directions. For all PROC MIXED F tests the df are 1/34000.

3. Results

3.1 Hormone Patterns X Phase X Day Effects

Least square means and standard errors of mood scores for PROC MIXED interaction effects are presented in Figures 1-3.

3.1.1 Nor X Cor X Phase X Day Effects on Happy

Significant interactions were found between Nor, Cor, and Phase for happy ($F = 4.35$, $p < .05$). As predicted higher ratings of happy were found during the L phase compared to the F phase for the pattern of lower Nor and lower Cor ($p = .033$). Higher ratings of happy were also found for the pattern of lower Nor and higher Cor compared to lower Nor and lower Cor ($p = .038$) and to higher Nor and higher Cor ($p = .009$), but only during the F phase. Ratings of happy for these two patterns (lower Nor and lower Cor during the L

phase, and lower Nor and higher Cor during the F phase) were also significantly higher compared to some other patterns of hormones in different phases (ps = .010 - .038, see Figure 1).

3.1.2 Nor X Cor X Phase X Day Effects on Sad

Significant interactions were found between Nor and Cor for sad ($F = 15.76$, $p < .0001$). Higher ratings of sad were found for the pattern of higher Nor and higher Cor in contrast to lower Nor and higher Cor ($p < .0001$) and higher Nor and lower Cor ($p = .001$). Higher ratings of sad were found for the pattern of lower Nor and lower Cor in contrast to the pattern of lower Nor and higher Cor ($p = .013$). See Figure 2.

3.1.3 Nor X Cor X Phase X Day Effects on Tired

Significant interactions were found between Nor, Cor, Phase, and Day for tired ($F = 5.63$, $p < .025$). Higher ratings of tired were found during the F phase compared to the L phase for the pattern of lower Nor and higher Cor ($p = .002$), but only for the off day.

Lower ratings of tired were found for the pattern of lower Nor and higher Cor compared to lower Nor and lower Cor ($p = .007$) and to higher Nor and higher Cor ($p = .002$), but only for the L phase during the off day. Lower ratings of tired were found for pattern of lower Nor and lower Cor compared to lower Nor and higher Cor ($p = .004$) and to higher Nor and higher Cor ($p = .003$), but only for the L phase during the work day. Higher tired mood was found for the work day compared to the off day during the L phase for the lower Nor and higher Cor hormone pattern ($p = .001$).

Significant differences in ratings of tired among hormone patterns in different phases and days are presented in Figure 3 (ps = .008 - .036).

4. Discussion

Our previous paper introduced a new arousal-related homeostatic hypothesis of mood regulation [34]. The hypothesis considers the joint impact of stress hormones, sex

hormones, and environmental context (level of contextual demand or stress) on arousal level, which in turn determines mood fluctuations. In a field where the impact of various biological and social factors are often analyzed separately, this approach considers the possibility that various combinations of biological and psychosocial variables can contribute to general arousal level - invest with energy, withdraw energy, or suppress activity which in turn affects mood states.

The current findings of HPA and SAM hormone patterns support the hypothesis and show that an increase in number of arousal-related factors (e.g., higher levels for both SAM and HPA daytime hormones) or a decrease in these factors (e.g., lower levels for both SAM and HPA daytime hormones) was associated with an increase in negative mood or a decrease in positive mood. Higher ratings of sad and tired and lower ratings of happy were found when SAM and HPA hormones were both high or both low. Additional arousal-related factors such as a phase of menstrual cycle can dampen (follicular phase) or magnify (luteal phase) the arousal-related effects of stress hormones on mood. When both SAM and HPA hormones were low, there were increased ratings of happy and decreased ratings of tired during the high arousal luteal phase but not during the follicular phase. In contrast to the off day, the level of arousal associated with the work day (i.e., occupational stress) in combination with the high arousal luteal phase increased the arousal level, leading to a decrease in the mood tired for the low arousal pattern of stress hormones during that condition.

The current study detected more arousal-related mood effects for norepinephrine level change as compared to cortisol. However, this effect needs further study as it was observed only for the moods happy and tired but not for sad. For instance, high norepinephrine during the high arousal luteal phase determined significantly lower happy mood irrespective of level of cortisol, but happy mood ratings showed only a tendency to lower

level for high cortisol during the luteal phase. This difference may be explained by the differential sensitivity of moods to arousal changes in central systems affecting mood. Compared to some negative moods, the mood happy may be more sensitive to small changes in general arousal. The arousal-related difference may explain the poor correlations between negative and positive mood ratings in some environmental contexts (see [42]). Future studies need to investigate how the validity of mood or emotional scales of general arousal fluctuation is affected by the integrated impact of energy metabolic (e.g., glucose and fatty acids), autonomic (e.g., heart rate, blood pressure), hormonal, environmental, and cognitive processes.

In general, the findings do not support Frankenhaeuser's proposal [1] on the relation between catecholamines and cortisol under different conditions of arousal and affect. An elevation in either catecholamines or cortisol accompanied by increases in another HPA or SAM system is an indication of negative emotion or distress. Moreover, the combination of low levels of both SAM and HPA hormones also indicated negative emotion. Mild arousal compensated for by other arousal-related factors (e.g., menstrual cycle phase and/or work stress) improved mood condition. Thus, the present findings interrelating hormone patterns and mood changes are consistent with our predictive model of the homeostatic arousal-related regulation of affect.

The current findings are in accord with a recent cross-sectional study in another sample of women, which showed that state anxiety measured by the Spielberger Anxiety Inventory was higher in subjects with lower epinephrine level during the follicular phase and with higher epinephrine level during the luteal phase compared to higher epinephrine level during the follicular phase and lower epinephrine level during the luteal phase [45]. Imbalances in stress and sex hormone interaction evoke emotional or mood symbolic "messages", signalling the need for behavioral control (rest, sensation avoidance, sensation

seeking) to redirect general arousal to a medium or homeostatic level [34]. Thus, any hormonal, metabolic, environmental, or cognitive activity can be related to mood valence (negative or positive) and mood dimension (sad, stress, anger etc.) based on their contribution to general arousal level. Following the hypothesis, emotions and mood are proposed to be an attribute of a central arousal system, which integrates arousal contributions from different external (e.g., dangerous or safe situations context) and internal (e.g., metabolic and hormonal activity) factors. In this instance, mood or emotion is a signal to consciousness about state of or shift to integrated arousal imbalance (negative affect) or balance (positive affect).

The arousal concept we have used for the interpretation of results considers biological and environmental effects on mood changes. Although the literature provides an opposite causal explanation of the interaction between moods and hormones, lack of control of temporal progression of cognitive, physiological, and emotional processes may obscure the true nature of their interaction. Any stress hormonal activity may be only an element in the cognitive and physiological chain of arousal cascade involving different fast (e.g., eye-blink, breathing, and heart rate) and slow (e.g., smooth muscle) reactivity processes. An affective feeling seems to be a conscious response to the arousal background of the cascade of different successive physiological and cognitive processes.

The findings of the present study underscore the importance of hormonal activity and other psychological and physiological factors associated with general arousal in the regulation of mood. Moreover, on the basis of other findings [34, 46 - 50], we can speculate that the arousal-related mechanism of negative mood regulation comes into play as a driving force to determine behavior when autonomic control fails to cope with arousal-related somatic and metabolic disturbances. Thus, low arousal negative mood can motivate normal or pathological sensation-seeking behavior (e.g., stimulant drug abuse, impulsive

behavior, and aggression), and high arousal negative conditions can determine sensation-avoidance behavior (e.g., sedative drug abuse and phobias). These findings refine our understanding of the common mechanisms associated with mood and psychosomatic disorders and attribute them to "disorders of arousal."

These processes of arousal regulation should be considered in the design of treatment interventions. Individuals who are in a high arousal condition may need comfort-related social support and various cognitive and other interventions for stress reduction and relaxation. In contrast, individuals who are in a low arousal condition may need activity-oriented social support and activation techniques such as physical activity for well-being. For instance, recent studies found that highly anxious subjects preferred avoidant behavior (i.e., passive-coping strategy) in a mildly stressful environment, which, in turn, was associated with lower activity of the SAM system. In contrast, low anxious subjects preferred an active-coping strategy. Similar hyperactivity of the HPA system occurred in both groups [51]. Thus, aside from the effects on mood, a person's proneness to a passive or active coping strategy may be another indication of arousal balance or imbalance.

The clinical relevance of such a differentiation is highlighted by findings, which suggest distinct responses to pharmacological treatments in different subtypes of depression: some patients are better responders to selective serotonin re-uptake inhibitors, others to tricyclic antidepressants [52]. Indeed, studies of depressed patients have shown that various subtypes of depression are associated with differential (very high or very low) levels in contrast to moderate levels of a complex of arousal-related factors, such as the arousal-producing neuropeptide corticotropin-releasing hormone (CRH) and norepinephrine in the locus coeruleus [53]. Whereas the melancholic subtype characterized by increased arousal, anxiety, insomnia, and weight loss was associated with increased CRH function and the hypernoradrenergic state, other subtypes (atypical, seasonal) were

associated with features of hypoarousal, fatigue, hypersomnia, and hyperphagia and had decreased CRH activity with consequent decrements of HPA function and the hyponoradrenergic state. Gold and Chrousos [53] proposed that optimal functioning of the central nervous system (CNS) requires that core stress system components remain within a carefully-maintained (i.e., homeostatic) range, and that deficits in CNS function can occur in the context of either a hyperactive or a hypoactive locus coeruleus (norepinephrine) and CRH system.

The homeostatic hypothesis suggests that pharmacological correction of mood and pathological self-regulated mood behaviors (e.g., drug abuse and risky behavior) may be achieved by adjustment of general arousal via effects on metabolism of hormones and neurotransmitters of different neuro-humoral systems. For example, in alcohol-dependent patients, naltrexone improved negative mood condition related to abstinence by stimulation of the inhibited activity of the HPA axis after alcohol withdrawal [54]. Subjects with attention-deficit/hyperactivity disorder (ADHD) or bipolar and atypical depression may have an innate deficit in internal sources for general arousal (e.g., hypoarousal condition related to low levels of corticosteroids and catecholamines). This deficit via negative mood as a driving force leads them to seek instant arousal stimulation (e.g., reward, pleasure), which determines impulsivity in their behavior (e.g., intolerance for reinforcement delay). In contrast, the presence of internal sources of hyperarousal related to intensive rumination in melancholic depression blocks an impulse for motivated behavioral activity and leads to rigid and automatic perseverative and obsessive-compulsive behavior. Thus, in one kind of conditions (e.g., atypical depression), a correction should be directed to creation or reactivation of inner arousal sources, but in another type of conditions (e.g., melancholic depression) treatment should be related to suppression of over-activated sources of arousal. In patients with ADHD, the psychostimulant drugs amphetamine and methylphenidate

reduce impulsive behavior via activation of dopamine neurotransmission [55]. In contrast, some dopamine D1 and D2 receptor antagonists increase impulsive behavior. The α2 adrenoceptor agonist clonidine inhibits noradrenergic activity and increases impulsivity, but noradrenergic reuptake inhibitors, such as desipramine and atomoxetine, have an opposite effect. Thus, the peripheral and central hormonal and neurotransmitter systems may be targets for arousal regulation to diminish negative mood and to maintain normal behavior. The concept of psychopharmacological treatment as a therapy of general arousal disorder could help refine the choice of drugs used for the treatment of mood and behavioral disorders.

Central arousal changes determined by cognitive appraisal of internal (memory) and external (environmental context) state, by personality traits (e.g., anxiety and hostility), or by peripheral physiological processes (e.g., glucose metabolism, estrogen activity) can evoke emotional or mood alterations [33 - 35, 45, 56]. For instance, sex hormones (e.g., estrogen) and certain environmental conditions (e.g., occupational stress) modulate central arousal level directly via a number of neurotransmitter systems [35, 57], as well as via reactivity of HPA and SAM hormones [35, 40, 58], which in turn may determine mood variability and behavior [32, 35].

Although the present study would be more conclusive if the combinations of factors proposed to contribute to moderate levels of arousal were shown to be associated with moderate levels of perceived arousal, the previous [34] and current findings showed that a higher level of perceived arousal, as indicated by ratings of tired, was also related to a moderate level of overall arousal. Indeed, in the luteal phase during the work day, the relationship between perception of energy (tired mood) and changes of the hormone pattern looks linear. However, when the concomitant condition changes to less arousal (the luteal phase during an off day or the follicular phase during the off day), the relationship becomes

nonlinear.

The current study was limited to healthy female nurses with specific job demands and to particular hormone patterns and mood ratings that may not fully represent variations in all women. The methods of study should be extended to women with mood and other disorders. Although the observed differences in mood reports were relatively small in magnitude, they were sufficiently consistent to yield significant effects by conservative statistical test. A direct manipulation of stress hormone patterns will help further explore the nonlinear causal model of interaction between physiological arousal and mood. The healthy status of the current sample of subjects may have limited the range of arousal and the ability to demonstrate that moderate arousal is associated with positive mood, low negative mood, and high energy [34]. In other samples of subjects, other analytic methods should demonstrate whether this curvilinear association is related to the full range of a single arousal factor or whether this association is determined only by intersection of multiple arousal-related systems.

In conclusion, by using real-time assessments of mood we have shown that the experience of moods is associated with daytime HPA and SAM hormone patterns in interaction with phase of the menstrual cycle and environmental stress. This interplay of factors suggests the need to develop and refine common arousal-related models of the regulation of mood and bodily systems and of risk for neuropsychiatric and psychosomatic disorders.

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Figure 1. Mean mood rating for Happy as a function of arousal pattern. Nor = Norepinephrine: High, Low; Cor = Cortisol: High, Low; Day: Both days; Phase = Menstrual Cycle Phase: F = Follicular, L = Luteal. Numbers at each point (diamond) indicate that the mean for that arousal pattern differed significantly from the designated other arousal conditions.

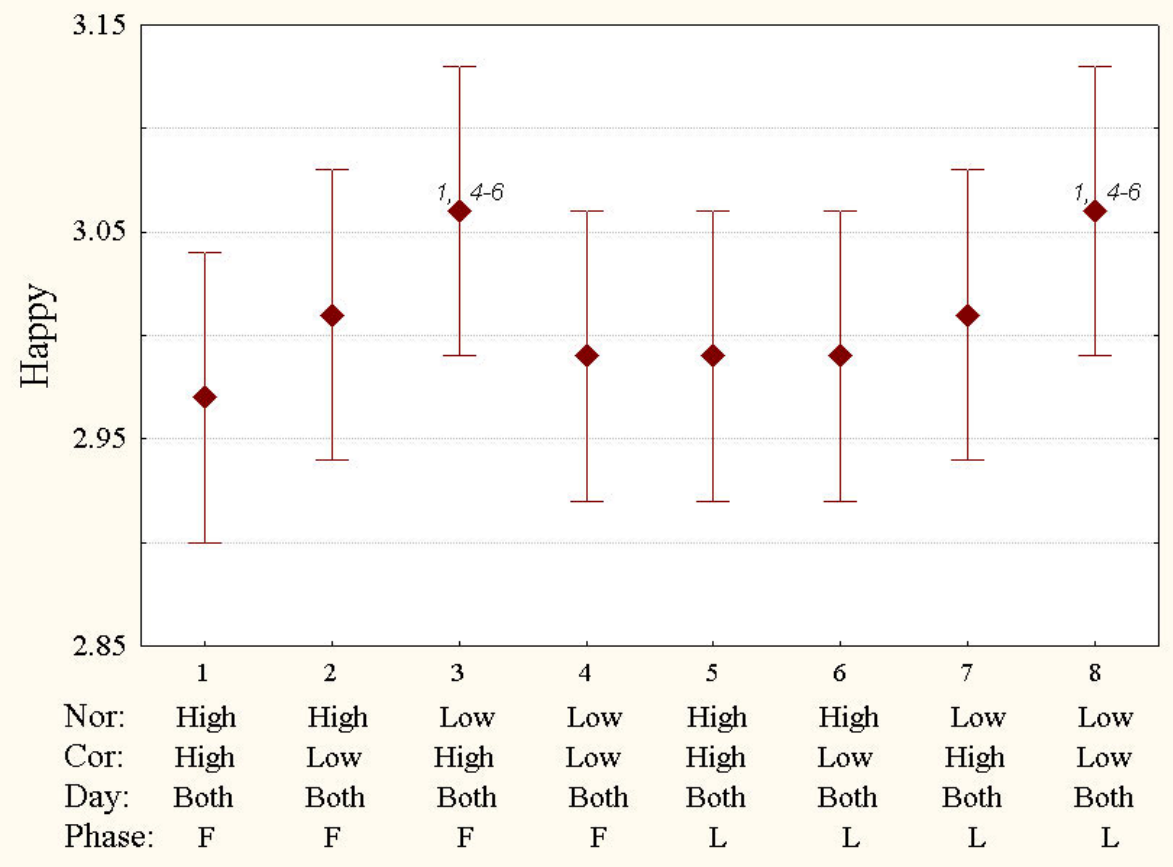

Figure 2. Mean mood rating for Sad as a function of arousal pattern. Nor = Norepinephrine: High, Low; Cor = Cortisol: High, Low; Day: Both days; Phase = Menstrual Cycle Phase: Both phases. Numbers at each point (diamond) indicate that the mean for that arousal pattern differed significantly from the designated other arousal conditions.

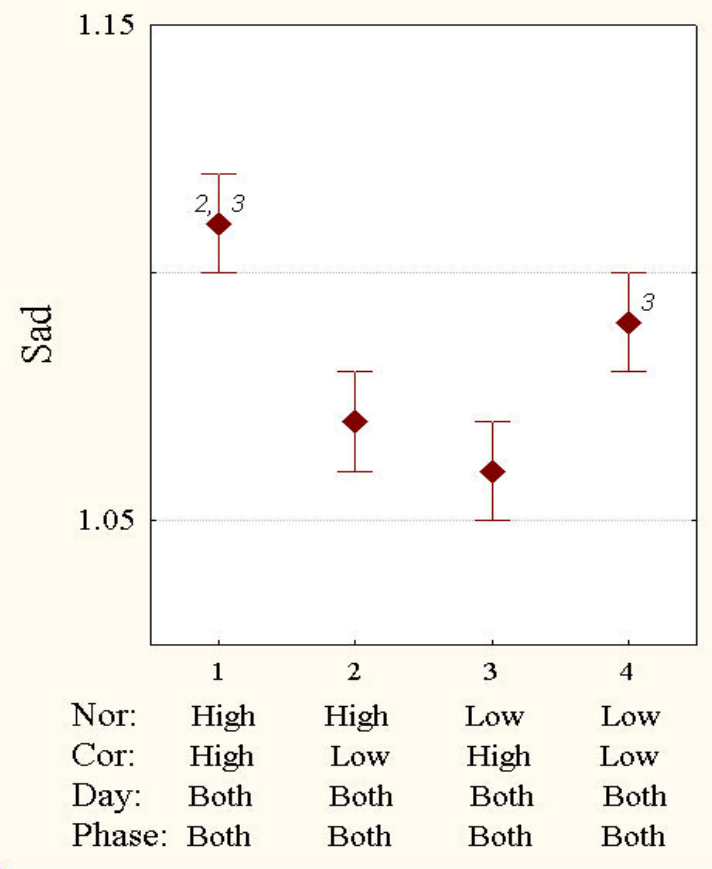

Figure 3. Mean mood rating for Tired as a function of arousal pattern. Nor = Norepinephrine: High, Low; Cor = Cortisol: High, Low; Day: Work, Off; Phase = Menstrual Cycle Phase: F = Follicular (Panel A), L = Luteal (Panel B). Numbers at each point (diamond) indicate that the mean for that arousal pattern differed significantly from the designated other arousal conditions.