

Nature's Clocks and Human Mood: The Circadian System Modulates Reward Motivation

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Existing literature on reward motivation pays scant attention to the fact that reward potential of the environment varies dramatically with the light/dark cycle. Evolution, by contrast, treats this fact very seriously: In all species, the circadian system is adapted to optimize the daily rhythm of environmental engagement. We used 3 standard protocols to demonstrate that human reward motivation, as measured in the dynamics of positive affect (PA), is modulated endogenously by the circadian clock. Under naturalistic conditions, 13.0% of PA variance was explained by a 24-hr sinusoid. In a constant routine protocol, 25.0% of PA variance was explained by the unmasked circadian rhythm in core body temperature (CBT). A forced desynchrony study showed PA to align with CBT in exhibiting circadian periodicity independent of a 28-hr sleep/wake cycle. It is concluded that the circadian system modulates reward activation, and implications for models of normal and abnormal mood are discussed.

Keywords: positive affect, light/dark cycle, adaptation

Twenty years ago, it was proposed that the circadian system may influence human reward motivation (Clark, Watson, & Leeka, 1989; Thayer, Takahashi, & Pauli, 1988). This hypothesis has significant implications for normal and abnormal reward function. However it has been largely overlooked because of the methodological challenges it invokes: Demonstration of a daily rhythm is straightforward, but verification of endogeneity is a significant interdisciplinary challenge.

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Reward Activation, Positive Affect, and Circadian Function

A family of related theories asserts that human behavior is influenced by two fundamental motivational systems (e.g., Carver, 2004; Corr, 2004; Davidson et al., 2002; Depue & Collins, 1999; Fowles, 1994). A reward system is proposed to underpin appetitive engagement with the environment, whereas a threat or aversive system explains withdrawal or vigilant inaction. The reach of this “two-system” paradigm is exceptionally broad, generating research into motivation, emotion, personality, and psychopathology (see reviews, Carver, 2004; Urosevic, Abramson, Harmon-Jones, & Alloy, 2008).

The neurobiology of reward-related motivation involves a range of neural structures including the left prefrontal cortex (Davidson et al., 2002), amygdala, orbitofrontal cortex and anterior cingulate cortex, which comprise key afferent and efferent projections of the mesolimbic dopaminergic system (Depue, Luciana, Arbisi, Collins, & Leon, 1994). The processing of reward-related information by this network impacts on dopaminergic cell function, which is synchronized in the striatum (Haber, Kim, Maily, & Calzavara, 2006). The threat system is subserved by the amygdala and the septo-hippocampal system (Fox, Henderson, Marshall, Nichols, & Ghera, 2005; McNaughton & Corr, 2004).

There is disagreement about the affect-level implications of reward and threat activation (e.g., Carver, 2004; Perkins, Kemp, &

Corr, 2007), but it is most commonly argued that activation of the reward system is experienced as the mood state positive affect (PA), whereas activation of the threat system is experienced as negative affect (NA; see, Watson, Wiese, Vaidya, & Tellegen, 1999). The variables PA and NA are reliably measured by self-report, enabling practical assessment of reward and threat activation in humans.

The reward potential of the environment varies with solar time, and an organism's fitness is enhanced by its being primed for environmental engagement when the likelihood of rewards is high (daytime for diurnal species, Wehr, 1990).¹ In all species, including humans, the endogenous circadian system is adapted for this purpose (Moore-Ede, 1986). A sensible inference, then, is that activity of the human reward system (and therefore subjective PA) is partly determined by timing information generated by the circadian clock located in the hypothalamic suprachiasmatic nucleus (SCN). Conversely, circadian variation in NA is not expected because any predictability of threat stimuli does not compensate for the high energy requirements of threat response activation (Watson et al., 1999).

Circadian modulation of reward in humans warrants systematic attention because the hypothesized relationship has significant implications for research into normal and pathological mood states. In animals, the involvement of the circadian system in reward activation has been investigated from a range of brain/behavior perspectives (e.g., Abarca, Albrecht, & Spanagel, 2002; Andretic, Chaney, & Hirsh, 1999; Cain, Ko, Chalmers, & Ralph, 2004; Dudley et al., 2003; Garcia et al., 2000; McClung et al., 2005; Ralph et al., 2002; Reick, Garcia, Dudley, & McKnight, 2001; Sleipness, Sorg, & Jansen, 2005, 2007). Demonstration of normative circadian variation in the uniquely human variable PA would provide the strongest evidence to date that a circadian-reward adaptation is conserved in humans, a contingency that has received inadequate attention in reward research. Furthermore, prominent models of mood disorder are premised on dysregulation of either circadian function (e.g., Wirz-Justice et al., 2005) or reward function (e.g., Urosevic et al., 2008). Compelling evidence for circadian-reward moderation would suggest that dysregulation of a higher order interactive system may be a productive target for new models of mood disorder pathogenesis (for some candidate hypotheses, see Murray, 2006).

Existing Evidence Base and Its Limitations

Data from a range of studies are broadly consistent with the hypothesis that reward activation is subject to circadian control. A diurnal PA rhythm has been demonstrated in three nycthemeral studies (Clark et al., 1989; Porto, Duarte, & Menna-Barreto, 2006; Watson et al., 1999). A similar waveform was found in the related variable energetic arousal in seminal research by Thayer (1987, 1989). The diurnal PA rhythm also has been shown to parallel the circadian rhythm in core body temperature (CBT) using a constant routine (CR) design (Murray, Allen, & Trinder, 2002). Using more rigorous methods, circadian variation has been demonstrated in subjective alertness (Van Dongen & Dinges, 2005) and a happy-sad measure (Boivin et al., 1997), both of which are located close to PA in mood factor space (Watson & Tellegen, 1999).

Although suggestive, methodological limitations render existing studies inconclusive. Measurement of a diurnal mood rhythm

under normal sleep-wake conditions can describe periodicity, but cannot address the question of endogeneity.² The CR method can test for rhythmicity in the absence of exogenous periodicity but introduces the confound of sleep deprivation (Redfern, Waterhouse, & Minors, 1991). The forced desynchrony protocol (FD, Dijk et al., 1997) circumvents sleep deprivation and can test for the existence of 24-hr periodicity dissociated from the sleep-wake cycle. A limitation of the FD is its questionable generalizability to naturalistic settings.

The Present Project

The aim of this project was therefore to provide a strong test of the hypothesis that reward activation, as measured by PA, is under circadian control, and the secondary hypothesis that activation of the threat system (measured by NA) is not. The project design included three studies and addressed four key methodological challenges, as described next.

First, the project was informed by research into the structure of human mood. The variables PA and NA are psychometrically sound constructs that align with the two-system paradigm. However, a complexity of the PA/NA pairing for the current purposes is the activation component of both variables (Watson et al., 1999): The known circadian rhythm in general alertness (Van Dongen & Dinges, 2005) might explain any observed circadian variation in PA (indeed, alert is an item in standard measures of PA; Watson, Clark, & Tellegen, 1988). To address this potential confound, alongside PA and NA we measured Valence from the alternative Activation/Valence model of mood (Russell & Carroll, 1999), and subsidiary analyses were conducted to ensure that observed circadian variation in PA was paralleled in this related measure of positive mood, relatively uncontaminated by alertness.³

¹ The balance of reward versus threat is an alternative environmental variable that may have influenced evolution (Silver & Lesauter, 2008). The present argument is unaffected by this issue: Although reward activation is reactively moderated by environmental rewards only, it is possible that reward functioning in its predictive mode has been adapted to account for the balance of reward versus threat probabilities.

² Rhythms with a 24-hr period can be generated by external periodic cues, but to be deemed circadian, a rhythm must be internally generated (endogenous) and sustain in the absence of environmental periodicity (Moore-Ede, 1986). The existing literature has provided grounds for skepticism about putative mood periodicities, which have sometimes proven false (Stone, Hedges, Neale, & Satin, 1985), exaggerated (Murray, Allen, & Trinder, 2001), or overly biologicistic (Dalglish, Spinks, Golden, & du Toit, 2004).

³ The strategy of testing for parallel variation in Valence permitted investigation of whether adapted circadian variation is unique to the mood variable PA, a question with implications for the relative ecological validity of the two competing rotations of mood space (Green & Salovey, 1999). The alternative strategy of statistically removing the alertness dimension from PA was rejected on the grounds that activation is fundamental to the unipolar mood dimensions in the PA/NA rotation of mood space. Our approach to parsing positive mood and alertness is premised on the accepted circumplex description of mood (Green & Salovey, 1999), but we acknowledge that causal relationships between the two phenomena are not understood. Dopaminergic pathways, for example, are implicated in both positive affect and arousal/alertness rhythms (see also, Harris & Aston-Jones, 2006; Monti & Monti, 2007).

Second, the challenge of analyzing repeated measurements of mood nested within individuals was addressed using multilevel modeling (MLM, also called *hierarchical linear modeling*), a relatively new statistical approach ideal for quantifying human biological rhythmicity (Van Dongen, Vitellaro, & Dinges, 2005). MLM properly accounts for within-person (Level 1) and between-person (Level 2) variance in longitudinal data, allows for nonindependence of mood observations, provides more precise parameter estimates than ordinary least squares regression and can accommodate missing data (Van Dongen, Olofsen, Dinges, & Maislin, 2004). The primary advantages of MLM over repeated-measures analysis of variance (ANOVA) are generation of precise (often more conservative) estimates of the temporal profile shared across subjects and quantification of individual variability around this shared profile (for recent application to mood research, see Peeters, Berkhof, Delespaul, Rottenberg, & Nicolson, 2006). To our knowledge, no existing tests of circadian modulation of mood have used MLM, leaving them unable to model the impact of between-person differences and vulnerable to Type I error.⁴

Third, a multimethod approach was used to avoid the limitations of any single protocol. In Study 1, eight 2-hr PA and NA reports per day were obtained during normal activities across 7 days. The distinctive feature of Study 1 was its naturalistic design, permitting the signal of a diurnal rhythm to be tested against the “noise” of noncircadian determinants of PA and NA. In Study 2, mood was assessed hourly over 30 hr of continuous wakefulness using a CR protocol. In contrast to Study 1, Study 2 measured PA and NA in an unvarying physical and social environment such that an observed 24-hr variation could not be attributed to exogenous factors. Further evidence for endogeneity was sought by testing whether the predicted 24-hr rhythm in PA paralleled the unmasked rhythm in CBT, the gold standard measure of SCN output (Van Dongen & Dinges, 2005). In Study 3, a forced desynchrony (FD) protocol was used to independently assess circadian and homeostatic/wake dependent influences on variation in hourly PA and NA. The FD protocol is important because it can test for 24-hr periodicity that is sustained even when dissociated from the sleep–wake cycle (Czeisler et al., 1999).

Finally, in a test of the assumption that PA variation represents reward activation in the circadian context, Study 3 included a physiological measure of reward activation, the Fowles gambling task (Fowles, 1988). The Fowles task is a potentially rewarding motor task, in which participants receive financial rewards for accuracy and speed (Colder & O’Connor, 2004). Fowles and others (e.g., Fowles, Fisher, & Tranel, 1982; Iaboni, Douglas, & Baker, 1995) showed that heart rate (HR) under the task is sensitive to the reward value associated with success and HR under the Fowles task has been used as a measure of reward system activation. Reaction time in reinforcement tasks may also index reward activation (Leue & Beauducel, 2008), and reaction time under the Fowles task was used here as a second objective measure of reward motivation.

Study 1 Method

Participants

To control for age-related effects on circadian function (Monk, Buysse, Reynolds, Jarrett, & Kupfer, 1992), age range for partic-

ipation was 18 to 30 years, a restriction that also applied in Studies 2 and 3. In all three studies, participants were enrolled tertiary students, and exclusion criteria were working on a shift schedule, use of mood-altering medication or drugs (excepting caffeine and alcohol) and presence of a physical or mental disorder. In Study 1 only, gender was controlled, with female gender selected on the grounds that women may on average be more adept at making fine distinctions about subjective states (Feldman Barrett, Lane, Sechrest, & Schwartz, 2000). One hundred participants were recruited by snowball sampling to generate an availability sample for Study 1, with 1 participant failing to complete. The final sample contained 99 participants (age: $M = 21.5$, $SD = 3.0$).⁵

Materials and Equipment

Due to the requirement for multiple mood reports each day, brief measures of PA and NA were created by abbreviating the well-validated Positive and Negative Affect Scales (PANAS; Watson & Clark, 1997; Watson et al., 1988). Following Clark et al. (1989) the 20 items of the PANAS were classified into four positive affect and five negative affect mood categories (as originally identified by Zevon & Tellegen, 1982). Based on the original factor loadings of Zevon & Tellegen (1982), one adjective from each of these nine categories was then selected. Thus, the abbreviated PA scale contained four adjective items (*excited, interested, determined, and active*) and the NA scale contained five (*upset, guilty, scared, hostile, and jittery*). In the present data set, coefficients of internal reliability were adequate at every time point for PA (across 56 administrations, mean $\alpha = .77$) and NA (mean $\alpha = .64$). At each administration, participants also gave ratings on the adjectives *happy* and *sad* (Valence was calculated as *happy* minus *sad*). Presentation of the 11 adjectives was randomized across reporting events. Participants rated how they were feeling “right now” on a 5-point Likert scale (1 = *very little/not at all*; 5 = *extremely*).

Procedure

Palm Pilot (m130) hand-held computers running Experience Sampling Program software (ESP [www.experience-sampling.org], Christensen, Feldman Barrett, Bliss-Moreau, Lebo, & Kaschub, 2003) were used to present items and record responses. Mood was rated every 2 hr between 08:00 and 22:00 for 7 days. Computers were programmed to sound an alarm to indicate a rating session. Participants were allowed 60 min to begin their responses to the alert and 20 s to complete each item. Clock time of response was confirmed by a time stamp automatically recorded by the ESP software. Participants were randomized to commence Study 1 on a weekday or weekend to counterbalance potential day-of-week effects on mood.

⁴ It is not uncommon for studies to calculate a parameter to represent an individual’s periodic mood behavior and subsequently correlate this with a trait measure (Jankowski & Ciarkowska, 2008; Murray, Allen, Rawlings, & Trinder, 2002). The weakness of this approach is that individual difference variance is not simultaneously included in the test for the hypothesized periodic effect.

⁵ The data of Study 1 were analyzed from a different perspective to form the basis of an argument about diurnal mood variation in depression. This argument was published in Murray (2007).

Data Analytic Strategy

In all studies, MLM was conducted with the SPSS Linear Mixed Models procedure (SPSS Inc., Chicago, IL). Hypothesis testing was based on models with the predictors present as both fixed (within-subject) and random (between-subjects) effects. Predictor variables for the circadian modulation hypothesis were a 24-hr cosinor function of time (Study 1),⁶ and the unmasked 24-hr rhythm in CBT (Study 2). In Study 3, the independent effects of circadian time (operationalized in CBT) and homeostatic effects (time since sleep) were jointly modeled (following the accepted two process model of sleep regulation; Dijk & Franken, 2005). In each study, intercept-only and unconditional growth models were fitted first to assess the need for multilevel modeling and to provide a reference against which predictors' effects could be quantified (Tabachnick & Fidell, 2007). Restricted maximum likelihood estimation was used in all analyses, with the criterion for statistical significance set at $p < .05$. All tests were conducted as two-tailed, with the exception of analysis of Level 2 effects in MLM, which are necessarily one-tailed, because they test whether variance is greater than expected by chance. Intercepts at both Level 1 and 2 were included in all models and were significant in each case. Plotting of predicted values against observed PA was used to confirm adequacy of models for each participant. To permit comparison with existing literature, repeated-measures ANOVA was also conducted. In all studies, the outcome was identical across analytic approaches so the more precise MLM findings are the focus here.

Study 1 Results

Missing data were haphazardly distributed across the 56 time points (mean missing: 6.7%, range: 0.0% to 13.1%), and across participants (mean missing: 6.6%, range: 0.0% to 19.6%). Identical findings were generated with and without missing value replacement, so the analyses presented here are of the former data.

Multilevel analyses found significant diurnal periodicity in PA (cosine curve, $F(1, 98) = 136.08, p < .001$, estimate = 3.01; sine curve, $F(1, 98) = 84.75, p < .001$, estimate = 2.23). Between-subjects (Level 2) differences in cosine and sine terms were also significant in the model (Wald $Z = 3.13, p < .005$ and Wald $Z = 5.18, p < .001$, respectively). The model containing predictors of periodicity provided an effect size of 13.01% over the null model. Subsidiary analyses also found significant periodicity in valence scores (cosine curve, $F(1, 96.63) = 29.52, p < .001$, estimate = 2.27; sine curve, $F(1, 98.12) = 43.36, p < .001$, estimate = 2.24).⁷

When data were aggregated across days and participants, the diurnal rhythm in PA was well fit by a 14-hr portion of a 24-hr sinusoid as assessed by least squares nonlinear regression ($R^2 = .84, p < .001$). This curve had a peak at 16:00, and (projected) trough at 04:00 (see Figure 1).

Also as expected, MLM found no evidence of 24-hr periodicity in NA (cosine curve $F[1, 98] = .48, ns$, sine curve, $F[1, 98] = .06, ns$). Figure 1 demonstrates the absence of periodicity in the aggregate NA data, and the large number of outlying values at each time point.

Study 1 Discussion

As predicted, MLM analyses found significant diurnal variation of sinusoidal form in PA ratings across the waking day. In line

with existing research (e.g., Watson et al., 1999), aggregated PA was found to peak in the early afternoon, plateau, and then decline in the late evening. Demonstration of a parallel rhythm in Valence suggested that the observed circadian variation in PA does not reduce to the known circadian variation in general alertness.

The MLM-derived effect size for periodicity in PA was 13.01%. By way of comparison, a recent large N study found extraversion to predict less than 9% of variation in momentary PA (Lucas, Le, & Dyrenforth, 2008), whereas correlates such as exercise and social interaction (unaided by shared method variance) explain less than 6% (Clark & Watson, 1988).

Also as hypothesized, NA did not exhibit significant diurnal variation. Rather, NA variation was erratic across participants and time, consistent with its putative reactive nature and the assumed unpredictability of threat.

A limitation of the study was the female-only sample, but the findings are in accord with mixed-gender studies (e.g., Watson et al., 1999), suggesting that they are likely to generalize. It can be concluded from Study 1 that, in the context of exogenous determinants of mood and individual differences in response, time of day is a significant predictor of PA but not NA ratings.

Study 2 Method

CR Protocol

In the CR procedure, light, temperature, noise, posture, activity, mealtimes, and sleep are controlled to "unmask" the endogenous circadian component of a 24-hr rhythm (Rietveld, Minors, & Waterhouse, 1993). Here, two different 30-hr conditions were used to counterbalance sleep deprivation effects. The evening condition commenced at 17:00 and finished at 23:00 the following day. The morning condition commenced at 10:00 and concluded at 16:00 the following day.

Participants

The inclusion criteria of Study 1 applied in Study 2, with the exception of the gender control. To avoid confounds due to menstrual cycle (Leibenluft, Fiero, & Rubinow, 1994), female participants in Study 2 completed the experiment during the follicular phase (as assessed by self-report at screening and additionally confirmed on the day of the CR). The protocol was completed by 12 participants (8 women; age $M = 22.1$ year, $SD = 3.4$; morning condition $n = 4$, evening condition $n = 8$).

Materials and Equipment

The variables PA and NA were measured hourly on the 10-item PA and NA scales of the PANAS. As in Study 1, valence scores

⁶ In this special case of repeated measures MLM, the presence of 24-hr periodicity is determined by a significant fit of the data to a sinusoidal curve. The standard polar transform is used to estimate amplitude and phase parameters of a sinusoidal curve by reparameterizing linear cosine and sine terms (for a recent application to mood research, see, Hasler, Mehl, Bootzin, & Vazire, 2008). A limitation of this linear approximation to nonlinear curve fitting is the restricted interpretation of parameters at Level 2.

⁷ Additional analyses also confirmed the expected synchrony between PA and Valence in all three studies.

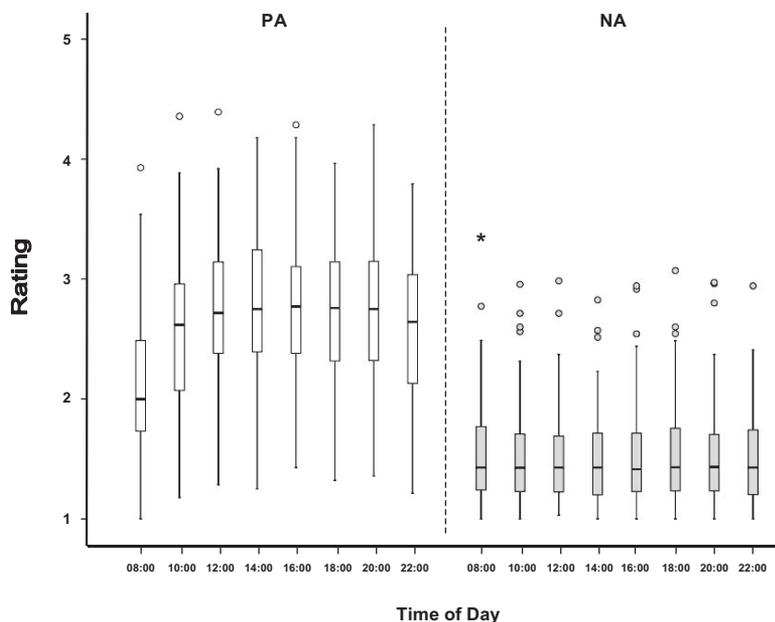


Figure 1. Boxplots of positive affect (PA) and negative affect (NA) ratings (average rating per item) for eight time points across the waking day, averaged across 7 days of reporting ($N = 99$). Circles and asterisks represent outliers and extreme values, respectively.

were derived from *happy* and *sad* ratings made at the same time points. In Studies 2 and 3, CBT was continuously measured using a disposable Mallinckrodt Monitherm rectal probe, and logged at 1-min intervals on the Mini-Mitter Mini-Logger 2000 (Respironics, Sydney).

Procedure

A normal day–wake/night–sleep rhythm was imposed prior to the CR, so the period of sleep deprivation was longer in the evening condition. The CR was conducted in the University of Melbourne sleep laboratory, where lighting (<20 lux in participants' angle of gaze) and temperature (21 °C) were kept constant. During the CR, participants were recumbent in bed and remained awake. Small 250-calorie meals were served every 2 hr, water was always available, and participants could walk to the bathroom as needed. The CR protocol demands that participants stay awake, and informed consent includes discussion of the right to withdraw from the study during the protocol, particularly if sleep deprivation becomes stressful. Participants are permitted to read, study, converse, or watch movies, and sleep is further discouraged through interaction with the experimenters.

To minimize the confounding effect of adjustment into and out of the CR, the middle 24-hr period of data were analyzed, generating 25 hourly mood reports. There were no missing data in this window. Morning and evening conditions were collapsed for hypothesis testing. The unconditional growth model for PA found a significant linear trend, so this term was a covariate in all models.

Study 2 Results

As predicted, MLM analysis collapsing across morning and evening conditions found significant 24-hr periodicity in PA at Level

1, cosine curve ($F[1, 11.24] = 27.22, p < .001$, estimate = 2.46). The sine term was nonsignificant, $F(1, 10.84) = .55, ns$, suggesting that individual differences in phase were not required in the model: The effect size for the model containing only a cosine term was 17.6%. Subsidiary analyses found comparable sinusoidality in valence (cosine curve, $F[1, 11.01] = 12.022, p < .01$, estimate = 4.45; sine curve, $F[1, 10.95] = .27, ns$). Also as expected, NA showed no sinusoidal variation, $F(1, 10.34) = 1.85, ns$.

Investigation of the relationship between PA and CBT found a significant Level 1 association, $F(1, 11.04) = 19.92, p < .005$, estimate = 8.53. Significant between-subjects differences in this relationship were also observed at Level 2 (Wald $Z = 1.65$, one-tailed, $p < .05$). Compared to the null model, inclusion of CBT in the prediction of PA produced an effect size of 25.0%.

When aggregated across participants, the morning condition PA rhythm was well described by a 24-hr sine curve ($R^2 = .65, p < .001$, trough at 05:28, Figure 2). An aggregate 24-hr sinusoidal rhythm was also found in the evening condition ($R^2 = .44, p < .001$, trough at 06:52, Figure 3). Under morning and evening conditions, aggregate PA demonstrated significant zero-order time series correlations with aggregate CBT ($r = .58$ [raw], $r = .95$ [fitted] and $r = .66$ [raw], $r = .79$ [fitted], respectively).

Study 2 Discussion

In a CR protocol, not only is the physical environment constant, but physical activity is restricted and opportunities for social interaction are relatively constant. Therefore, a 24-hr variation in PA under the conditions of Study 2 cannot be explained as a reactive consequence of a daily rhythm in rewarding events. As in Study 1, variation in PA was strongly synchronized with the mood variable Valence, suggesting that the observed PA periodicity

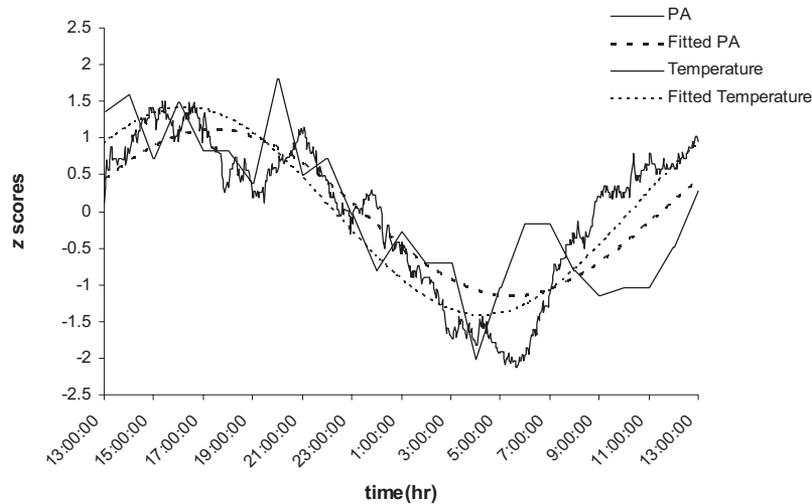


Figure 2. Mean hourly positive affect (PA), core body temperature and fitted 24-hr sinusoids (morning condition, $N = 4$).

cannot be explained by its general alertness component alone. Consistent with circadian modulation, PA exhibited both large effect-size 24-hr periodicity of sinusoidal form, and a strong association with the gold-standard continuous measure of circadian output (CBT under CR). Neither of these effects was significant for NA. As in Study 1, there was evidence of significant Level 2 differences in the relationship between CBT and PA, which can be interpreted as individual differences in the circadian component of PA.

Aggregate analyses also showed PA to have marked sinusoidality and synchrony with CBT. This pattern of findings is identical to the sole comparable study (Murray, Allen, & Trinder, 2002), offsetting concerns about the small sample used here. The trough of the fitted PA sinusoid fell 2 to 3 hr later than the trough in the

temperature rhythm, a phase relationship that has been noted for performance/alertness rhythms in relation to CBT (Van Dongen & Dinges, 2005).

In the absence of manipulation of circadian function, causality has not been demonstrated here. However, the data suggest that PA periodicity under normal sleep-wake conditions may be a component of a complete circadian oscillation that is unmasked by preventing sleep.

Study 3 Method

FD Protocol

Participants were maintained on a 28-hr day (with approximately 9:20 of sleep and 18:40 awake each “day”) for 8 normal

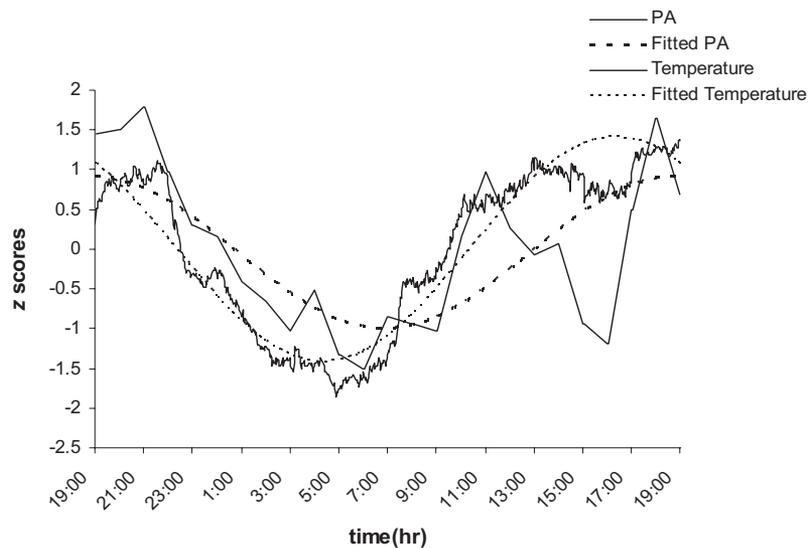


Figure 3. Mean hourly positive affect (PA), core body temperature, and fitted 24-hr sinusoids (evening condition, $N = 8$).

24-hr days. Under this schedule, the circadian oscillator continues to cycle at approximately 24 hr and hence desynchronizes from the sleep–wake cycle that adopts the enforced 28-hr period.

Participants

Exclusion criteria were as for Study 2, with the addition of a personal/family history of hypertension or cardiovascular/respiratory disorders. Fifteen participants (7 women, age $M = 21.93$ years, $SD = 3.19$) completed the protocol.

Materials and Equipment

As in Study 2, PA and NA were measured each waking hour on the PANAS. Valence was measured at the same time points on a *happy–sad* visual analogue scale. The Fowles task was used in Study 3 to generate objective measures of reward activation. The Fowles task is a potentially rewarding motor task, in which five lights randomly illuminate and can be turned off by tapping an adjacent button. Participants receive a small financial reward (5 cents) for each correct tap in a 2-min trial. HR was calculated from the R-R ECG intervals (the time between the R wave of two heartbeats), recorded from Einthoven Lead-2, digitized at 2 kHz. Participants completed five trials per block, mean normalized HR was calculated for each block (after discarding the first 2-min trial), and HR data were transformed into deviation from individual participants' mean across the FD. We also calculated normalized median reaction time under the Fowles task as an additional operationalization of reward motivation (lower reaction time corresponds to greater reward activation; see Leue & Beauducel, 2008). The Fowles task was completed a total of 43 times across the FD, once every 2 to 3 hr (2, 4, 7, 9, 11, 16 hr after rising) per 28-hr day.

Procedure

The schedule ran for 8×24 hr days, allowing for an adaptation period and for six sleep–wake (28 hr) and seven circadian (~ 24 hr)

cycles to be studied. Participants were tested individually in the laboratory environment described for Study 2. A consistent sleep–wake schedule was prescribed for 2 weeks before the protocol.

The unconditional growth model identified a linear effect of hours in study for HR, so this term was a covariate in MLM analyses. To permit comparison with previous FD research, results of repeated measures ANOVA are also presented: data were collapsed into 6×3 -hr bins for the hours awake factor and $6 \times 60^\circ$ bins for the circadian phase factor. The fitted minimum of the circadian temperature cycle was assigned to 0 degrees for the circadian phase factor.

Study 3 Results

Analyses using ANOVA found PA to vary significantly with circadian phase, $F(5, 70) = 7.47$, $p < .001$, partial $\eta^2 = .35$ (Figure 4). The aggregate circadian rhythm in PA (cosinor analysis $R^2 = .94$, $p < .001$) paralleled the circadian rhythm in CBT (cosinor analysis $R^2 = .94$, $p < .001$), with both peaking at sextant 180° to 240° . Beyond the marked circadian effect, hours awake was significantly associated with PA in a linear decreasing trend, $F(5, 70) = 36.81$, $p < .001$, partial $\eta^2 = .72$ (Figure 5). The interaction between the two time variables (hours awake and circadian phase) in the prediction of PA was also significant, $F(25, 350) = 2.12$, $p < .005$, partial $\eta^2 = .13$. The relationship between the two time variables and HR during the Fowles task was effectively identical to that for PA (Figures 4 and 5).

The pattern of findings was replicated using MLM analysis: PA was significantly associated with the circadian rhythm in CBT and hours awake (CBT: $F(1, 14.54) = 22.75$, $p < .001$, estimate = 8.84, hours awake: $F(1, 14.71) = 35.41$, $p < .001$, estimate = -0.33). Between-subjects (Level 2) differences in CBT and hours awake factors were also significant (Wald $Z = 2.06$, $p < .05$ and Wald $Z = 2.27$, $p < .05$, respectively). The model containing both CBT and hours awake explained 24.23% of the variance over the null model for PA.

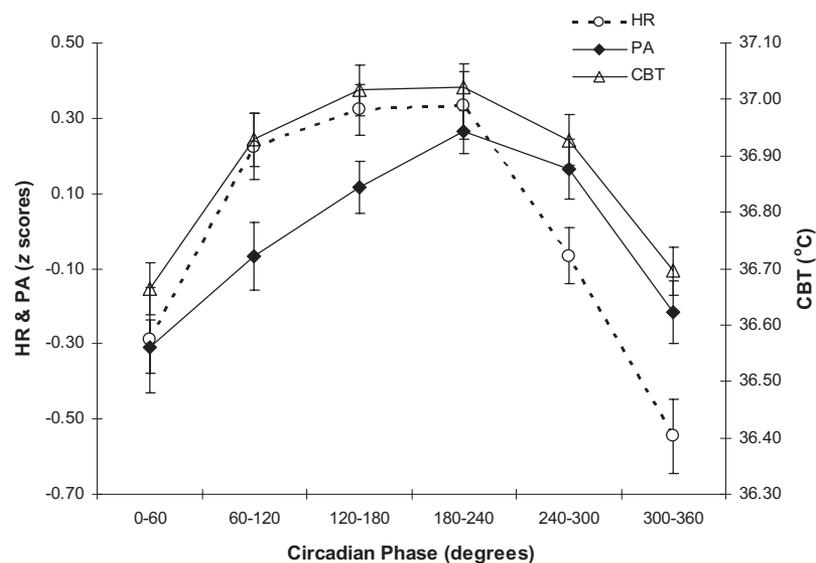


Figure 4. Mean (\pm SEM) positive affect (PA), heart rate (HR), and core body temperature (CBT) plotted against time circadian phase ($N = 15$).

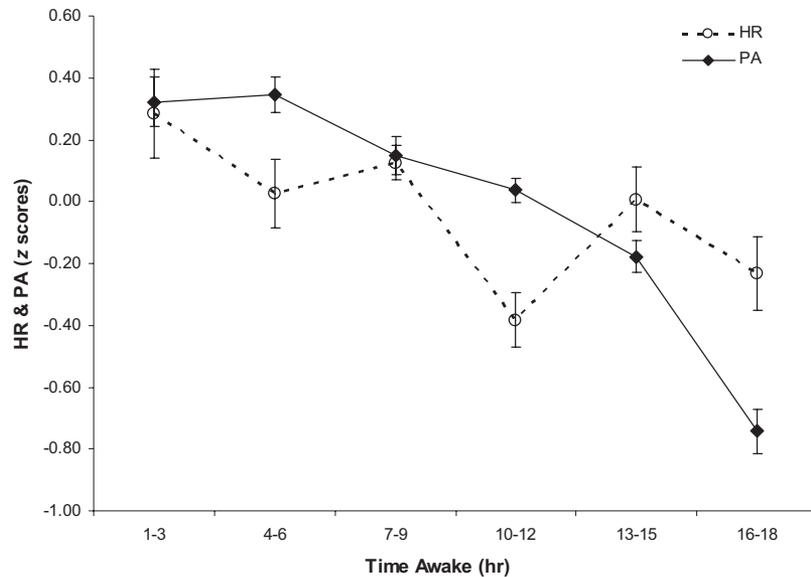


Figure 5. Mean (\pm SEM) positive affect (PA) and heart rate (HR) plotted against time hours awake ($N = 15$).

Findings were very similar when HR under the Fowles task replaced PA as the dependent variable in MLM analyses. Both CBT and hours awake were significant predictors of HR, CBT: $F(1, 16.34) = 25.28, p < .001$, estimate = 10.72, hours awake: $F(1, 13.31) = 5.76, p < .05$, estimate = -0.23 . Both factors were also significant at Level 2 (Wald $Z = 2.07$, two-tailed $p < .05$ and Wald $Z = 1.66$, one-tailed, $p < .05$, respectively). The model predicting HR from CBT and hours awake explained 20.68% additional variance over the null model. Similarly, normalized median reaction time under the Fowles task was significantly associated with CBT, CBT: $F(1, 11.49) = 15.58, p < .005$, estimate = -1.30 , and approached significance with hours awake, ($F[1, 11.21] = 3.79, p = .077$, estimate = 0.02).

There was no evidence for 24-hr periodicity in NA when predicted from the circadian rhythm in CBT ($F(1, 12.83) = .72, ns$, estimate = -0.11) or hours awake ($F(1, 13.85) = 1.17, ns$, estimate = -0.01). As in the earlier studies, dynamics of PA strongly paralleled the dynamics of Valence: Valence was significantly associated with the circadian rhythm in CBT ($F(1, 13.36) = 7.07, p < .05$, estimate = 0.94) and hours awake ($F(1, 14.23) = 4.70, p < .05$, estimate = -0.01).

Study 3 Discussion

The FD protocol of Study 3 permitted independent assessment of circadian and sleep-wake determinants of PA and NA. As expected, ANOVA and MLM analyses showed that PA dynamics under FD conditions are impacted by circadian and time-since-sleep processes. Most important, it can be concluded that even when the sleep-wake cycle (and the behaviors it gates) are experimentally driven to a non-24 hr period, 24-hr periodicity remains significant in PA and this periodicity is synchronized to the circadian rhythm in CBT. It is difficult to explain this pattern of findings without recourse to an endogenous circadian rhythm in PA. As in Studies 1 and 2, findings in relation to PA were clarified

by evidence for parallel variation in Valence, and absence of periodicity in NA.

Average normalized HR in response to the Fowles task showed a circadian rhythm that, like PA and CBT, peaked at sextant 180° – 240° . In MLM analyses, PA and HR exhibited similar dynamics in relation to circadian and homeostatic predictor terms.⁸ This pattern of findings, along with the similar outcomes based on reaction time under the Fowles task, is consistent with the assumption that self-reported PA represents reward activation in the circadian context (see more below). More important, the effect sizes for prediction of PA and HR were comparable, suggesting that our central hypothesis was not advantaged by focusing on the subjective facet of reward activation.

It is possible that the periodicity in HR identified under the Fowles task reflects an underlying variation in resting HR, which is unrelated to the motivational properties of the task.⁹ Indeed, resting HR in this data set was synchronous with CBT (Trinder et al., 2007) and thus with HR during the Fowles task. Although the present design cannot exclude the possibility that a generalized circadian rhythm (in, e.g., metabolic function) explains the Fowles HR periodicity, evidence of its covariation with subjective PA and valence and response time under the Fowles strongly suggests a more specific effect due to reward activation.

General Discussion

Given its multimethod design, the project generated remarkably orderly findings. The hypothesis that the circadian system modu-

⁸ The homeostatic linear effect was negative (see Figure 5), aligning with findings for subjective alertness and neurocognitive performance, which also decrease with increasing homeostatic sleep drive (Van Dongen & Dinges, 2005).

⁹ We thank an anonymous reviewer for this suggestion.

lates PA was supported by demonstration of (a) a diurnal rhythm discerned above the noise of other endogenous and exogenous determinants of PA in a naturalistic setting (Study 1), (b) a 24-hr rhythm synchronous with the circadian rhythm in CBT in the absence of environmental variation in reward (Study 2), and (c) independent circadian and homeostatic effects on PA and replication of the synchrony between circadian rhythms in PA and CBT in the absence of sleep deprivation (Study 3). These findings were extended by demonstrating that circadian modulation of PA is paralleled by circadian modulation of a plausible physiological measure of reward-related arousal (Study 3), consistent with the assumption that PA represents reward activation in the circadian context.

The predicted dissociation was also found: NA ratings exhibited no periodicity and no association with CBT, consistent with the presumed reactive operation of the threat system, and the argument that superiority of the PA/NA rotation of mood space is supported by differential correlates of PA and NA (Watson et al., 1999). Two caveats on this conclusion should be noted, however. First, measurement of circadian variation in NA may be subject to Type II error because of the range restrictions seen in self-reported NA (see Figure 1). A provocation design would be useful to definitively rule out circadian variation in the threat system (this research should also consider the bifurcation of anxiety and fear in contemporary Reinforcement Sensitivity Theory; Perkins et al., 2007). Second, in a novel finding, circadian variation was also found in Valence, suggesting that adapted periodicity in mood may not be unique to PA. Perhaps because of its strong evaluative component, the variable Valence is not generally viewed from an adaptationist perspective (Russell, 2003), and so the possibility of a circadian component in Valence has not previously been tested. However, PA and *happy* show moderate cross-sectional correlations (Carroll, Yik, Russell, & Feldman Barrett, 1999), so it is unsurprising that a moderator of one also appears to moderate the other.

The findings are consistent with existing theory and data mentioned above, and it seems reasonable to conclude that the circadian system modulates human reward motivation. As measured in PA variation, the size of the effect is large, and larger than that found for better recognized predictors. It is demonstrable within individuals, as required by the hypothesis, but also appears in aggregated analyses. Humans are not slaves to this rhythm, of course—the majority of variance in PA remains unexplained by a circadian rhythm (Studies 1 to 3), an interacting homeostatic process is also a significant driver (Study 3) and as yet unexplored individual differences moderate the relationship (Studies 1 to 3). The pivotal conclusion nonetheless remains and has significant implications.

The circadian modulation of PA closely resembles known circadian modulation of subjective alertness and other neurocognitive variables. Like PA, circadian variation in these measures is approximately synchronized with the circadian rhythm in CBT (with peak performance circa the temperature maximum; Van Dongen & Dinges, 2005). More important, however, the data demonstrated that circadian variation in PA was synchronized with the unambiguous mood variable Valence. It appears therefore that PA (and positive mood states more broadly) constitute a distinctive addition to the group of higher cognitive functions whose variation is synchronized by timing information from the SCN. This is a

noteworthy finding because, unlike neurocognitive variables, PA represents the semantics or content of thought, not just its syntax (see, Matthews, 2000). Terms like *inspired* and *proud* are elements of PA; it is striking that such complex phenomenology is moderated by a primitive sunrise forecasting system.

The brain's reward pathways can be parsed into appetitive/dopaminergic and consummatory components, with the former being most clearly associated with positive affects and reward activation (Ashby, Isen, & Turken, 1999; Bressan & Crippa, 2005). In lower mammals, circadian modulation of reward seeking has been demonstrated behaviorally. For example, Sleipness and colleagues (Sleipness et al., 2005, 2007) showed differential response to rewarding stimuli in rats depending on zeitgeber time. These authors coined the term *reward potential* to describe the adapted tendency to be sensitive to rewards at times of day when reward seeking is most likely beneficial. In lower mammals, the brain pathways subserving this link are afferents from the SCN, which project via the paraventricular thalamic nucleus to the mesolimbic dopaminergic reward system (Sleipness et al., 2007). The present findings suggest that imaging investigations are now warranted to explore the conservation of these pathways in humans. Viewing reward activation as a dopaminergic phenomenon in humans also generates novel hypotheses about circadian variation in reward across the sleep phase: The timing of REM sleep is strongly modulated by the SCN (Czeisler, Buxton, & Khalsa, 2005), and REM is associated with elevated dopaminergic activity (Dahan et al., 2007; Lima et al., 2008).

By employing MLM to simultaneously model within- and between-subjects variance, novel evidence was found for interindividual differences in circadian modulation of PA. This discovery is important because individual differences in circadian parameters may have functional significance, particularly if they are shown to be trait-like (Murray, Allen, Trinder, & Burgess, 2002). There appears to be a species-wide circadian-reward adaptation, but the operation of this system differs across people, potentially providing clues about temperament and vulnerability to disorders of circadian-reward function.

Dysregulation of reward function and circadian function are believed to be two important pathways to mood disorder (Murray & Harvey, in press). The demonstration here of circadian modulation of reward activation is consistent with the existence of an integrated circadian-reward neurobiological system, dysregulation of which may be causally important in mood disorder.¹⁰ One potential locus for a functional circadian-reward system involves clock gene activity in brain reward centers. Roybal and colleagues (2007) showed that clock mutant mice display increased dopaminergic activity in the VTA, as well as behaviors homologous to mania (hyperactivity, decreased sleep, increase in the reward value of cocaine, etc.). These behaviors are normalized by administration

¹⁰ A number of circadian-reward pathogeneses warrant investigation, including abnormal alignment between circadian and homeostatic effects (Boivin et al., 1997) and weakened SCN input into the daily rhythm of engagement (Murray, 2007; Murray, Allen, Trinder, & Burgess, 2002; Murray, Judd, & Bullock, 2007). Given that the circadian system operates as an open loop, it has also been proposed that alterations in mood (and associated activities) are the starting point for disturbance of circadian function in vulnerable individuals (Healy & Waterhouse, 1995; Mistlberger, Antle, Glass, & Miller, 2000).

of lithium, and by expression of a functional CLOCK protein specifically in the VTA. More broadly, growing evidence for functional clock gene activity outside the SCN is consistent with the present argument for models of mood disorder that are premised on an integrated circadian-reward system.

The primary focus here on the subjective manifestation of reward activation in humans (PA) is defensible as a complement to data on the neurobiology of the circadian-reward system in animals. Although the core hypothesis was also supported in relevant objective data, a more complete approach would pay equal attention to psychological and biological aspects of reward activation. There is no agreed multilevel measure of human reward activation (e.g., Carlezon & Thomas, 2009; Naqvi & Bechara, 2009), but measurement of left frontal asymmetry would address concerns about the reward specificity of the objective findings here (e.g., Amodio, Master, Yee, & Taylor, 2008).

Conclusions

Within its limitations, the present project has generated strong evidence that the human reward system is primed by the circadian system. This finding extends animal research by demonstrating the moderation effect in subjective PA and related positive mood states. Time is a challenging variable to model, but hypotheses about reward motivation will improve when we accept, as evolution itself has done, that the planet's rotation is too important to ignore.

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