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Time-of-day differences and short-term stability of the neural response to monetary reward: A pilot study

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ABSTRACT

Human and animal studies indicate that reward function is modulated by the circadian clock that governs our daily sleep/wake rhythm. For example, a robust circadian rhythm exists in positive affect, which is lower in the morning hours and peaks in the afternoon. A handful of functional neuroimaging studies suggest that systematic diurnal variation exists in brain activity related to other functions, but no published human studies have examined daily variation in the neural processing of reward. In the present study, we attempt to advance this literature by using functional neuroimaging methods to examine time-of-day changes in the responsivity of the reward circuit. Using a within-person design and a functional magnetic resonance imaging (fMRI) monetary reward task, we compared morning and afternoon reward-related brain activation in a sample of healthy young adults within 24 h. Region of interest analyses focused on the striatum, and we hypothesized greater reward activation in the afternoon, concordant with the circadian peak in positive affect. Results were consistent with our hypothesis. In addition, we counterbalanced the order of morning and afternoon scans in order to explore the short-term stability of the neural response. Whole-brain analyses showed a markedly higher reactivity to reward throughout the brain in the first scan relative to the second scan, consistent with habituation to the monetary reward stimuli. However, these effects did not appear to explain the time-of-day findings. In summary, we report the first preliminary evidence of circadian variation in the neural processing of reward. These findings have both methodological and theoretical implications.

1. Introduction

Human and animal studies indicate that reward function is modulated by the circadian clock that governs our daily sleep/wake rhythm. Both positive affect, an experiential phenomenon related to activation of the reward system, and psychophysiologically assessed reward activation show clear 24-h rhythms, and these rhythms vary according to circadian timing (Boivin et al., 1997; Murray et al., 2009). The pattern of these rhythms—levels are lowest close to wake-up time, then rise to a peak in the late afternoon or evening before beginning to fall—roughly parallels the core body temperature rhythm. Furthermore, these rhythms are paralleled by the diurnal patterns of reward-related behaviors (e.g., socializing and alcohol consumption) (Arfken, 1988; Hasler et al., 2008). Rodent studies also support the circadian modulation of reward-related behavior and its underlying physiology within the reward circuit. Drug-seeking behavior, responsiveness to drugs of abuse, expression of the dopamine transporter, and the expression of circadian genes throughout the mesolimbic dopaminergic pathway all show 24-hour rhythms (Sleipness et al., 2007; Webb et al., 2009). However, no published human studies have examined daily variation in the neural processing of reward.

A handful of functional neuroimaging studies suggest that systematic diurnal variation exists in brain activity related to other functions, including time-of-day variations in the activity of the motor cortex (Tamm et al., 2009; Peres et al., 2011), in hypothalamic and brainstem activation related to maintaining attention (Schmidt et al., 2009), and in brain reactivity to cognitive interference (Schmidt et al., 2012). In addition, several studies have compared brain glucose metabolism during morning and evening wakefulness in healthy adults, adults with major depression, and adults with primary insomnia (Buysse et al., 2004; Germain et al., 2007; Hasler et al., 2012). In all three studies, distinct diurnal patterns of relative glucose metabolism emerged in regions relevant to reward function, including the medial prefrontal cortex, anterior cingulate cortex, and striatum. Notably, increased evening activity within striatal regions associated with reward processing was a common thread across all three studies.

In the present pilot study, we take the first step in attempting to advance this literature by using functional neuroimaging methods to examine time-of-day changes in the responsivity of

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Table 1
Demographics and sleep data ($n=11$ unless otherwise indicated).

Age	21.51 ± 1.72 years, range = 19–24
Sex	4 males / 7 females
Race	6 Caucasian, 3 African-American, 1 Asian-Pacific, 1 refused to provide info
PSQI	1.82 ± 1.17, range = 0–4
CSM	34.20 ± 4.86, range = 28–42
Sleep diary ($n=10$)	
Sleep onset (clock time)	1:01 ± 0:54, range = 23:44–2:31
SOL (min)	8.04 ± 1.66, range = 0.00–15.00
WASO (min)	2.90 ± 0.88, range = 0.00–6.63
Sleep offset (clock time)	8:36 ± 0:49, range = 7:50–10:05
TST (h)	7.53 ± 0.97, range = 5.25–8.33

Notes: PSQI = Pittsburgh Sleep Quality Index; CSM = Composite Scale of Morningness; SOL = Sleep onset latency; WASO = Wake after sleep onset; TST = Total sleep time.

the reward circuit. Using a within-person design and a functional magnetic resonance imaging (fMRI) monetary reward task, we compared morning and afternoon reward-related brain activation in a sample of healthy young adults within 24 h. The within-person design provides greater statistical power than between-person designs more typically employed in fMRI studies, and it is also powerful in minimizing the contribution of individual differences, by allowing each participant to serve as his/her own control. We focused on the striatum, hypothesizing greater reward activation in the afternoon, consistent with the circadian peak in positive affect (Boivin et al., 1997; Murray et al., 2009). Secondarily, we performed a preliminary exploration of the test-retest reliability of our reward paradigm, albeit confounded within time-of-day. Given the dearth of test-retest reliability data on fMRI reward tasks re-administered less than 7 days apart (Fliessbach et al., 2010; Plichta et al., 2012) and the importance of understanding the reliability of widely used fMRI techniques, we counterbalanced the order of the AM and PM scans in order to examine the short-term stability of striatal response. In addition, this approach allowed us to detect any potential effects of task habituation.

2. Methods

2.1. Participants and procedures

These data come from a pilot study designed to examine daily changes in reward-related brain function using fMRI. The study was approved by the University of Pittsburgh Institutional Review Board, and all participants provided written, informed consent.

Participants included 11 healthy young adults (7 females), including five participants recruited from an ongoing study using fMRI to study the impact of sleep deprivation on affect regulation. All participants were free of major medical, sleep, or psychiatric disorders, based on a clinical interview and several standard sleep-related instruments, including the Pittsburgh Sleep Quality Index (PSQI; (Buysse et al., 1989)) and a daily sleep diary, which included items on bedtime, lights out (the time participants closed their eyes with their intention to fall asleep), sleep onset, sleep offset, sleep latency (interval from lights out until sleep onset), and wakefulness after sleep onset (amount of wakefulness between sleep onset and sleep offset). The diary was completed for a mean (± S.D.) of 7.50 ± 2.83 days per participant. No participants reported clinically-significant sleep disturbance based on the PSQI (PSQI < 6 for all participants) and mean sleep diary was consistent with this conclusion (see Table 1). Participants also completed the Composite Scale of Morningness (CSM; (Smith et al., 1989)) to assess individual differences in preferred sleep-wake timing (i.e., chronotype or morningness–eveningness). None of the participants reported an extreme chronotype based on the CSM. See Table 1 for demographic information.

The study included two fMRI scans.[1] Following the baseline assessment and a week on a stable self-selected sleep-wake schedule, participants underwent the two scans: one during the morning (on average, 1.56 h after habitual waketime; range = −0.10–3.80 h), and one during the afternoon (on average, 8.23 h after waketime; range = 6.62–10.80 h see footnote one).

The order of these scans was counter-balanced, such that six participants completed the morning scan first, and the afternoon scan later that day, and five participants completed the afternoon scan first, and the morning scan the next morning. All six of the AM–PM order participants completed both scans on the same day. Four of the five PM–AM order participants completed scans on consecutive days. The sole exception completed the PM scan as scheduled, but rescheduled the AM scan 13 days later.

On average, AM scans occurred at 10:11 (range = 7:32–11:47) and PM scans occurred at 16:51 (range = 15:06–18:38), with a mean difference in timing between AM and PM scans equal to 11 h and 40 min (range = 5.50–18.82 h[2]). Participants were asked to avoid naps, caffeine and alcohol use on scan days. Participants completed a guessing task with monetary reward during both the morning and afternoon scans.

2.2. fMRI monetary reward task

To probe patterns of neural activity in response to monetary reward, we used a card guessing fMRI paradigm. The block design paradigm consists of pseudo-random presentation of trials wherein participants played a card guessing game and received either positive or negative (i.e., win or loss) feedback for each trial. Participants were told that their performance on the game would determine the monetary reward received at the end of the study, earning $1 for each "correct" guess and losing $0.50 for each "incorrect" guess. Participants were unaware of the fixed outcome probabilities associated with each block until the entire study protocol was completed, at which time they were debriefed and compensated $10 for each completion of the reward task.

During each trial of this task, participants are given 3 s to guess, via button press, whether the value of a visually presented card would be higher or lower than 5 (index and middle finger, respectively). After a choice was made, the numerical value of the card was presented for 500 ms and followed by appropriate feedback (green, upward arrow for win; red, downward arrow for lose) for an additional 500 ms. Upon receiving positive feedback, subjects were required to respond via button press to collect the money for that trial (i.e., consummatory behavior). An inter-trial crosshair was then presented for 3 s, for a total trial length of 7 s. Each block consisted of five trials, with three "win" blocks each of predominantly positive feedback (80% correct) and three "lose" blocks of predominantly negative feedback (80% incorrect), interleaved with three control blocks. During control ('neutral') blocks, participants were instructed to simply make alternating button presses during the presentation of an 'x' (3 s), which is followed by an asterisk (500 ms) and a yellow circle (500 ms), and then a crosshair (3 s). Each block was preceded by a 2-s instruction of "Guess Number" (for positive or negative feedback blocks) or "Press Button" (for control blocks), resulting in a total block length of 37 s and a total task length of less than 6 min.

[1] These were the first and second scans under normal sleep conditions. Two of the five participants recruited from the sleep deprivation study had already completed a fMRI scan and reward task under sleep-deprived conditions a respective 7 and 12 days beforehand. Removing these two participants from the (*footnote continued*) analyses did not result in substantive changes to the findings reported in Section 3.3 (all three clusters remained significant after correction for multiple comparisons).

[2] Including the 13 intervening days of the aforementioned participant that rescheduled their AM scan would raise the maximum scan time difference to 304.32 h. Dropping this participant from the AM-PM comparison (Section 3.2) resulted in findings that were in the same direction, albeit somewhat weaker (the VS cluster in the PM > AM contrast had the same peak voxel with a t-value = 4.49 and cluster size below the AlphaSim threshold at 52 voxels).