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Preliminary Communication

Circadian phase shifts and mood across the perinatal period in women with a history of major depressive disorder: A preliminary communication

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ABSTRACT

Background: Perinatal changes in maternal sleep patterns may modify circadian phase. Our objectives were to (a) measure changes in circadian phase and phase angle between salivary dim light melatonin onset (DLMO) and sleep onset across the perinatal period; and (b) prospectively examine associations between circadian measures and depressed mood in women with a history of major depressive disorder (MDD).

Methods: Twelve women (age ± SD = 26.9 ± 5 years) who fulfilled DSM-IV criteria for history of MDD (but not in a mood episode at enrollment) were studied from third trimester of pregnancy through postpartum week 6. Participants completed sleep diaries, wore wrist actigraphs and light sensors, and had mood assessed with the Hamilton Depression Rating Scale (HAMD-17) during 3 separate weeks of the perinatal period; they gave saliva samples at 33 weeks gestation and 6 weeks postpartum to determine DLMO phase.

Results: Nine women had DLMO phase shifts ≥30 min. On average ± SD, new mothers phase delayed 42 ± 80 min (range = 163 min phase delay to 144 min phase advance). The time interval between average actigraphic sleep onset and DLMO was shorter at 6 weeks postpartum compared to 3rd trimester in 9 of 12 women, indicating that most new mothers were going to bed closer to the onset of endogenous melatonin secretion. Circadian measures were associated with depressed mood at postpartum weeks 2 and 6.

Limitations: These data are preliminary findings from a small sample and require replication.

Conclusions: We observed individual differences in magnitude and direction of circadian phase shifts and their timing relative to sleep across the perinatal period. These measures were correlated with postpartum depressive symptoms. These preliminary data indicate that changes in perinatal circadian rhythms may contribute to the development of postpartum mood disorders.

1. Introduction

Previous research highlights changes in sleep behavior and sleep timing in the postpartum period, including increased daytime napping distributing sleep across the day (Signal et al., 2007; Swain et al., 1997) and later rise times in the weeks following delivery compared to third trimester. One group of 36 women followed with sleep diaries, for example, reported average delay in wake time of 52 min from 3rd trimester of pregnancy to 2–4 weeks postpartum (Wolfson et al., 2003).

Few studies have examined perinatal circadian rhythms. One cross-sectional study of postpartum women showed altered patterns of urinary 6-sulfatoxymelatonin excretion compared to non-pregnant, nulliparous controls; differences included blunted circadian rhythm amplitude along with elevated melatonin levels in daytime urine samples (Thomas and Burr, 2006). Another study compared plasma melatonin profiles in 2 groups—(1) depressed and non-depressed pregnant women near the end of third trimester and (2) depressed and non-depressed new mothers (Parry et al., 2008). Results showed lower average 24-h melatonin levels in depressed pregnant women compared to healthy controls; in contrast, depressed postpartum women exhibited higher melatonin levels than controls, with no significant difference in

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time of average melatonin onset or offset observed between depressed and non-depressed women in either group. We emphasize that all of these studies of melatonin secretion patterns in perinatal women were cross-sectional samples, and none examined differences in circadian phase or phase angle across the perinatal period.

We speculate that sleep pattern changes that occur in the early postpartum period alter light–dark exposure and may thus modify circadian phase. The primary aim of this study was to measure circadian phase before and after the birth of a child to examine whether women experience circadian phase shifts across the perinatal period. We hypothesized that women who delay their sleep also experience delays in salivary dim light melatonin onset (DLMO) phase at postpartum week 6 relative to 3rd trimester of pregnancy.

Given the growing body of work in perinatal sleep and postpartum depression, (e.g., Bei et al., 2010; Coble et al., 1994; Lee et al., 2000; Okun et al., 2009; Okun et al., 2011), our secondary aim was to explore whether circadian measures were associated with postpartum depressed mood in our sample of women with a history of MDD.

2. Methods

2.1. Participants

We recruited participants who telephoned the laboratory in response to flyers, brochures, newspaper advertisements, and a direct mailing. We studied women ages 18–40 who fulfilled DSM-IV criteria for history of MDD but who were not in a current mood episode at 33 weeks gestation calculated by last menstrual period. Mood disorder history and absence of a mood episode at enrollment were confirmed by a Structured Clinical Interview for DSM Disorders (SCID I/P, (First et al., 2002)). We excluded those with a primary Axis I diagnosis other than MDD; learning disability, mental retardation, or developmental delay; diagnosis of a primary sleep disorder (including insomnia); high risk pregnancy; current employment as night shift worker; disability that interfered with testing; current alcohol/drug dependence; expectation that infants would not be living in the home or would have a nighttime caregiver; and women taking hypnotics for insomnia. Women with comorbid anxiety disorders were not excluded. We did not select participants on the basis of parity, feeding plans, tobacco use, or use of antidepressants, anxiolytics, antipsychotics, or mood stabilizers. The Rhode Island Hospital and Women and Infants Hospital institutional review boards approved the study. Participants gave signed informed consent and were paid for participating.

2.2. Circadian phase measures

We measured dim light salivary melatonin onset phase (DLMO) at approximately 33 weeks gestation and 6 weeks postpartum. Participants wore wrist actigraphs and kept sleep diaries for 1 week before each DLMO phase assessment to record bedtimes and wake times (see below). Spring and fall DLMO phase assessments were completed at least 2 weeks after daylight savings time.

On the day of DLMO phase assessment, researchers went to participants' homes with a saliva collection kit that included labeled tubes, saliva sample log, and a scale to weigh samples. Participants also were given dark welder's glasses (Uvex, Smithfield, RI) to wear continuously during saliva collection to avoid light-induced melatonin suppression. Saliva was collected using Salivettes (Sarstedt, Nümbrecht, Germany) every 30 min from ~2.5 h before the predicted DLMO phase time to ~3 h after predicted DLMO phase, determined from sleep diary data (Burgess and Eastman, 2005). A researcher telephoned the participant at each sample time to prompt saliva collection and to confirm welder's glasses were worn. Participants were instructed to log the time and weight of each sample (target weight was 9 g including the Salivette to ensure adequate sample quantity). Participants refrigerated Salivettes overnight; samples were collected the next day, centrifuged, and frozen at −20 °F.

Saliva samples were assayed for melatonin using radioimmunoassay (Alpco, Salem, NH). We defined threshold for melatonin production onset as 4 pg/ml (Lewy et al., 1998; Lewy et al., 1999). Fig. 1 illustrates the circadian measures. DLMO phase was computed by linear interpolation between the times of saliva samples before and after the melatonin levels reached threshold. Phase shifts between 3rd trimester and 6 weeks postpartum were determined by subtracting the DLMO phase at 6 weeks postpartum from the 3rd trimester DLMO phase. Thus, a negative value indicates a phase delay shift (i.e., a later DLMO phase postpartum). We considered DLMO time changes larger than the 30-min saliva sample collection interval circadian phase shifts. The phase angle between DLMO and sleep pattern was calculated by subtracting DLMO time from sleep onset time averaged for the 7 nights before saliva collection. Thus, a positive value indicates the time interval after DLMO that sleep was initiated; larger values indicate falling asleep later relative to melatonin secretion onset.

Circadian phase *preference* was measured at enrollment with the Horne–Östberg Morningness–Eveningness Questionnaire (MEQ; Horne and Östberg, 1976); scores range from 16 to 86 with lowest scores indicating an evening (night owl) preference and highest scores a morning (early bird) preference.

2.3. Sleep and light measurements

Participants wore a wrist actigraph (Octagonal Basic or Micro Motionlogger Watch, AMI, Ardsley, NY) continuously on the nondominant wrist for 1 week each at ~33 weeks gestation and at postpartum weeks 2 and 6. (Settings were 1-min bins in zero crossing mode with a filter setting of 18). Activity data were analyzed using Action-W software (AMI) algorithm, which has been validated with polysomnography (Sadeh et al., 1994). We derived the following sleep measures from actigraphy: sleep onset time (first of 3 continuous epochs of sleep occurring after the bedtime reported on the sleep diary); sleep offset time (last epoch of 5 continuous epochs of sleep occurring before the wake time reported on the sleep diary); and sleep minutes (number of minutes of estimated sleep occurring between sleep onset and sleep offset).

We measured ambient light exposure with a Micro Light Sensor (AMI, Ardsley, NY) worn continuously pinned/clipped to the shirt or with the built-in light sensor on the Micro Motionlogger Watch (3 participants). Light data (lux) were analyzed with Action-W software; measures included the average and maximum levels over 24 h and during the actigraph-defined sleep periods.

In addition to wearing actigraphs/light sensors, participants completed a daily sleep/wake diary developed for perinatal women (Wolfson et al., 2003) and called into the laboratory's time-stamped voicemail each day when they woke up. Diary items include bedtime, rising time, amount of sleep, naps, and times when they removed the actigraph.

2.4. Mood measures

We assessed symptoms of depressed mood with the 17-item Hamilton Rating Scale for Depression (HAMD, Hamilton, 1960) performed by a trained, board-certified psychiatrist (KMS) at the