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Identification of changes in sleep across pregnancy and the impact on cardiometabolic health and energy intake in women with obesity

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Abstract

This prospective, observational study investigated changes in sleep and the effect on energy intake, gestational weight gain, and cardiometabolic health across pregnancy in 52 healthy pregnant women with obesity. Habitual sleep was assessed by wrist-worn actigraphy (time spent in bed; TIB, total sleep time; TST, and sleep efficiency) in early (13^0-15^6 weeks) and late (35^0-36^6) pregnancy. A change to habitual sleep was defined as change of one-half of the standard deviation of TIB and TST across six consecutive nights from early pregnancy. Energy intake and changes in weight, fasting glucose, insulin, and lipids across pregnancy were compared between women who changed sleep. During early pregnancy, TIB was 9:24±0:08h and varied by 1:37±0:07h across the six nights. TST and sleep efficiency significantly declined from early to late pregnancy (7:03±0:08h to 6:28±0:09h, $p<0.001$) and (76±0.1% to 71±0.2%, $p<0.001$), respectively. For women who increased TIB (n=11), fasting glucose decreased (−11.6±4.3%, $p<0.01$) across pregnancy and they had a trend towards decreased insulin (−57.8±33.5%; p=0.09) and HOMA-IR (−72.4±37.3%; p=0.06) compared to women who decreased TIB (n=13). Women who increased TIB had a significantly lower daily energy intake across pregnancy (−540±163 kcal; $p<0.01$) and tended to have less gestational weight gain (−147±88 g/week; p=0.10). Changes in TST did not affect plasma markers, energy intake or weight gain. The positive relationship between sleep and cardiometabolic health during pregnancy is explained in part by lower energy intake. We

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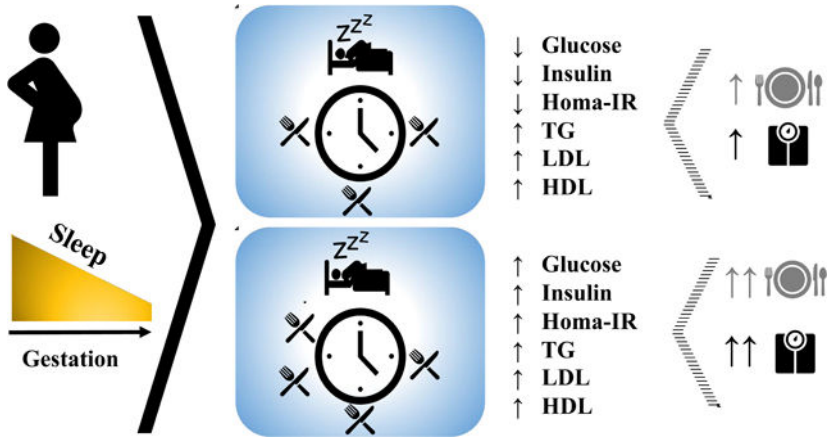
hypothesize lower energy intake is due to a prolonged overnight fast and a decrease in the time available for eating.

Graphical Abstract



Left: Factors of sleep (ie. sleep quality and duration) decline as pregnancy progresses. Women who increase time spent in bed (**center top**) throughout pregnancy show less deteriorations in cardiometabolic health compared to women who shorten time spent in bed (**center bottom**). ↑ indicates increase in fasting values from early to late pregnancy. ↓ indicates decrease in fasting values from early to late pregnancy. **Right**: Different cardiometabolic responses are hypothesized to be a result of increased eating occurrences and shortened overnight fast (**grey**) since these women evidence increased energy intake and gestational weight gain.

Introduction:

Pregnancy is a physiological event associated with well documented, progressive declines in sleep duration and sleep quality (Facco, Kramer, Ho, Zee, & Grobman, 2010; Lee, Zaffke, & McEnany, 2000). Inadequate sleep is related to declines in metabolic and cardiovascular health (St-Onge et al., 2016) and individuals with short sleep and sleep-related disorders (e.g. sleep disordered breathing) are more likely to have overweight and obesity. In pregnancy, shortened sleep coupled with progressive insulin resistance underscore the necessity to understand the direct and indirect relationships between sleep and adverse cardiometabolic outcomes. Relationships between sleep and cardiometabolic health are indeed evident in pregnancy but have not completely been explored (Facco, Grobman, et al., 2017; Facco, Parker, et al., 2017).

Large observational studies assessing sleep with objective methods such as wrist worn actigraphy have linked shortened sleep duration in pregnant women with increased incidence of gestational diabetes (Facco, Grobman, et al., 2017). While valuable, the assessment of sleep with actigraphy at a single time point during pregnancy and only after diagnosis of gestational diabetes omits potential dynamic changes in sleep that precede the worsening of glucose tolerance from being quantified (Abdul Jafar, Eng, & Cai, 2019). To our knowledge, very few studies use objective measurements of sleep across multiple trimesters (Martin-

Fairey et al., 2019; Tsai, Lee, Lin, & Lee, 2016) and, unfortunately these lack simultaneous evaluations of metabolic health biomarkers.

In non-pregnant adults, shortened sleep has been shown to enhance cravings for palatable foods and to increase hunger and appetite (Patterson et al., 2014). Therefore, sleep in pregnancy may interact with eating behaviors to support a novel mechanism that explains in part, increases in cardiometabolic risk factors with advanced gestation. Prior research also lacks objective measures of energy intake and eating behaviors to help understand the potential link between sleep and worsening cardiometabolic health across pregnancy.

The aim of this study was to test the overarching hypothesis that sleep (duration and quality) declines across pregnancy and corresponds to a deterioration in cardiometabolic health. A secondary aim was to assess if deteriorations in cardiometabolic health among those who decreased sleep duration may be explained by increased energy intake and changes in eating behaviors. To accomplish these aims we first characterized sleep patterns in early and late pregnancy using both actigraphy and self-reported sleep and second, we assessed if changes in cardiometabolic biomarkers, energy intake and eating behaviors differed between women who decreased or increased different components of sleep across pregnancy.

Materials and Methods:

Study design

This is an *a priori* planned secondary analysis of participants enrolled in a prospective observational study at the Pennington Biomedical Research Center designed to assess determinants of gestational weight gain in women with obesity (Most et al., 2019; Most, Vallo, Gilmore, et al., 2018). Wrist-worn actigraphy, self-reported sleep, assessments of eating behaviors, and plasma biomarkers were collected between 13 and 16 weeks (‘early’) and between 35 and 37 weeks (‘late’) gestation. The study was approved by the Pennington Biomedical Research Center Institutional Review Board and written informed consent was obtained from all participants prior to the initiation of procedures.

Participants

Eligible women were pregnant, 18 to 40 years of age, and with obesity (measured BMI ≥30 kg/m^2) at the screening visit (gestational age, <15 weeks). Women were excluded for smoking, alcohol or drug use, hypertension (SBP >160, DBP >90), diabetes (HbA1c > 6.5%), or use of medications that may affect body weight or energy intake. Of the 54 women who completed the study, 52 (96%) had actigraphy data from both early and late pregnancy and therefore were included in analysis.

Actigraphy sleep assessment

Sleep was quantified objectively by wrist-worn actigraphy (Actigraph GTX3+, Pensacola, FL) over six consecutive nights. The sleep assessment period corresponded with an assessment of free-living energy expenditure by doubly labeled water (described below). Wrist-worn actigraphy has been validated against polysomnography as an accurate and sensitive measure of night sleep and wakefulness (Marino et al., 2013). Accelerometers were

secured to the wrist of the non-dominant hand using hospital-style wrist straps which prevented the device from being removed for the entirety of the measurement period. Raw data were analyzed using an open-source R package (GGIR) for quantifying sleep without relying on a sleep diary (van Hees et al., 2018). Sleep was quantified as the absence of change in arm angle greater than five degrees for five or more minutes, during the sleep period time window. The sleep period time window is the 12 hours centered around the least active five hours of the 24-hour window based on ENMO (Euclidian Norm Minus One). In total, all 1440 minutes per day were used to detect the sleep period time window. Since time in bed does not equate to actual sleep time, time in bed (TIB) was expressed as the difference between sleep onset time and wake time. Total sleep time (TST) is the cumulative minutes of inactivity between sleep onset time and sleep wake time. Sleep efficiency is defined as the ratio between time spent sleeping and total time in bed (TST/TIB). Adequate nightly sleep duration was defined as a sleep duration greater than seven hours (Watson et al., 2015).

Over the six consecutive nights of measurement, we computed the night-to-night variability (standard deviation across all nights of measure) for each individual to indicate the regularity of TIB and TST. The night-to-night variability, which reflects habitual weekly sleep patterns, was then used to compute the change in habitual weekly sleep across pregnancy. We defined a change in habitual weekly sleep (TST and TIB) as an increase or decrease of at least one-half the early pregnancy (baseline) night-to-night variability. Women whose weekly habitual sleep change was within these bounds were classified to have no change in sleep across pregnancy.

Self-reported sleep assessment

Self-reported sleep was assessed using questionnaires administered under ideal conditions while the participant was residing overnight on the inpatient unit. Habitual sleep patterns including sleep onset and wake times and sleep duration on weeknights and weekends, time to fall asleep, and time spent awake were assessed using a study developed instrument. The Epworth Sleepiness Scale was used to evaluate daytime sleepiness (Johns, 1991). The Epworth Sleepiness Scale is a 9-item questionnaire in which participants rate how likely they are to “doze off or fall asleep” in eight different situations during the past four weeks and is scored on a 4-point Likert (0= no chance, 1= slight chance, 2= moderate chance, 3=severe chance). The lowest possible cumulative score is 0 (low daytime sleepiness) and highest possible score is 36, indicative of severe daytime sleepiness.

Anthropometrics

Body weight and body composition were measured after an overnight fast. Body weight was measured in a clinic gown on an electronic scale. Total weight gain from early to late pregnancy divided by the number of weeks between study visits was used to calculate rate of gestational weight gain in grams per week. Body fat mass was calculated using body weight, body volume by plethysmography (BODPOD®, COSMED, Concord, CA) and body water (mean estimate of using zero-intercepts of ^{2}H and ^{18}O-isotopes) (Most, Marlatt, et al. 2018). Fat-free mass was calculated as body weight minus fat mass.

Energy Intake

Energy intake was measured according to the intake-balance model as described (Most et al., 2019). Briefly, energy intake was calculated as the sum of total daily energy expenditure and changes in energy stores by the energy intake-balance method (Thomas et al., 2012). Free-living energy expenditure was measured over seven days by doubly labeled water (1.25g of 10% enriched ^{18}O and 0.10g of 99.9% enriched $^{2}H_2O$ per kg body weight) and energy deposition was calculated assuming densities of 9,500 kcal per kilogram of fat and 771 kcal per kilogram of fat-free mass (Most, Marlatt, Altazan, & Redman, 2018).

Diet quality including macronutrient composition (kcal from protein, fat, or carbohydrate), and the 2015 Healthy Eating Index (HEI) was evaluated with food photography. The HEI is a multi-component scoring system that evaluates fruit, vegetable, dairy, grain and protein, added sugars, solid fats and oils, and number of alcoholic drinks consumed related to the 2015–2020 Dietary Guidelines of Americans recommendations (Millen et al., 2015). In depth explanation of diet assessment procedures has been previously described (Most, Vallo, Altazan, et al., 2018). Briefly, for six consecutive days during the doubly labeled water assessment participants captured images of foods and plate waste using the SmartIntake smartphone application, which is a validated food photography method for diet quality (Martin et al., 2012). Days in which energy intake was >60% of energy expenditure measured by doubly labeled water were considered valid and included in the analysis. To calculate the HEI, the foods and beverages were first converted into the 37 USDA food pattern components using the Food Patterns Equivalents Database, which was used to evaluate food and beverage intakes of Americans with respect to the 2015–2020 A lower HEI is indicative of a poorer score (The Epidemiology and Genomics Research Program, 2018).

Eating behaviors were measured subjectively by validated questionnaire instruments. In early and late pregnancy, the eating inventory (EI), food craving inventory (FCI), and the mindful eating questionnaire (MEQ) were included in a single questionnaire packet completed under standardized conditions during an overnight stay on the inpatient unit. The EI evaluates three factors of eating behaviors: dietary restraint, disinhibition, and perceived hunger. A low score for the dietary restraint, and high scores for disinhibition and perceived hunger indicate less control of eating behaviors (A. J. Stunkard & Messick, 1988; A. J. Stunkard & Waterland, 1997). The FCI evaluated the magnitude of general food cravings as well as cravings for high-fat foods, sweets, carbohydrates/starches, and fast foods (White, Whisenhunt, Williamson, Greenway, & Netemeyer, 2002). A higher FCI indicates greater cravings. Lastly, the MEQ evaluates five subscales of mindful eating: disinhibition, awareness, external cues, emotional response, and distraction. Results are represented as a composite score, in which a higher value is indicative of mindful eating (Framson et al., 2009).

Cardiometabolic Biomarkers

Blood was drawn in the morning following an overnight fast and insulin (Immulite 2000, Siemens, Broussard, LA), glucose, triglycerides, low-density lipoprotein (LDL, Beckman DXC600, Beckman Coulter Inc, Brea, CA), and high-density lipoproteins (HDL, Trinity

DXC600, Trinity Biotech, Jamestown, NY) were measured in real-time in the clinical chemistry core laboratory. Insulin sensitivity was calculated as HOMA-IR.

Statistical analysis

Percent change for glucose, insulin, HOMA-IR, triglycerides, LDL, HDL, and eating behaviors were calculated from early to late pregnancy. Data are reported as mean ± SEM. Sleep time is reported in hours and minutes (HH:MM). Differences between early and late pregnancy sleep parameters (TIB, TST, and sleep efficiency) were analyzed using t-tests and within group comparisons (frequencies) for those who increased, decreased, or no change are reported. To test for differences in outcomes variables (glucose, insulin, HOMA-IR, triglycerides, LDL, HDL, eating behaviors, gestational weight gain) between three groups (increased, decreased, no change) for two dependent variables (TIB and TST) we used linear mixed models with group as the between-subject factor and enrollment BMI as a covariate to adjust for any effect of BMI on changes in outcomes. Post-hoc testing with Bonferroni adjustment was performed to determine intergroup differences. Due to only one participant increasing TST, only interactions between decreased and no change were reported for TST. All analyses were set as alpha≤0.05 as the predetermined level of significance. Analyses were carried out by a biostatistician using SAS/STAT software, Version 9.4 of the SAS System for Windows (SAS Institute Inc. Cary, NC, USA).

Results

Participants

Fifty-two women (27.4±0.7 years) with obesity (BMI: 36.3±0.7) were studied from early pregnancy until late pregnancy. Forty-six percent (46.2%) of the women were Caucasian, 46.2% were African American, and 7.6% classified as other. Majority of the women were employed (65.4%), married (61.5%), and approximately half were pregnant with their first child (48%).

Sleep measured by actigraphy

Sleep measured by actigraphy and self-report in early and late pregnancy are presented in Table 1. Participants wore the wrist accelerometer on average six nights in both early and late pregnancy. Only 55.8% of women during early pregnancy and 30.8% during late pregnancy achieved adequate nightly sleep of seven hours. On average, the sleeping duration is consistent during each observation period (Figure 1a and 1b). In early pregnancy, the average weekly time spent in bed (TIB) was 9:24±0:08h and varied 1:37±0:07h across the six nights. TIB and the night-to-night variability in TIB were unchanged in late pregnancy at 9:14±0:11h and 1:46±0:10h, respectively. Sleep onset and wake times did not change from early to late pregnancy. Total sleep time (TST) declined significantly from early to late pregnancy (early: 7:03±0:08h to late: 6:28±0:09h, $p<0.001$) as did sleep efficiency (early: 76±0.1% to late: 71±0.02%, $p<0.001$). Night-to-night variability for TST and sleep efficiency did not change across pregnancy. Changes to TIB across pregnancy were positively associated with changes in TST ($r=0.46$, $p=0.02$) and were inversely related to changes in sleep efficiency ($r=-0.68$, $p<0.001$).

Of the 52 women, 11 increased TIB from early to late pregnancy and 13 decreased TIB, with the remaining 28 women showing no change to TIB. Those who increased TIB throughout pregnancy spent 0:58±0:10h more time in bed in late pregnancy ($p<0.001$) while those who decreased TIB spent 1:46±0:09h less in bed. Only one participant increased TST while 26 decreased TST, at an average change of −0:38±0:13h ($p=0.004$ from early to late). The remaining 25 women had no significant change in TST (0:17±0:13h; $p>0.05$).

Self-reported sleep assessment

Using questionnaire instruments, self-reported sleep onset and wake time and sleep duration did not change throughout pregnancy. In early and late pregnancy there were no significant differences in these parameters between weekdays or weekend days. There was no change in average daytime sleepiness as measured by the Epworth Sleepiness Scale from early to late pregnancy.

Impact of sleep on cardiometabolic biomarkers

No baseline differences were observed between TST and TIB groups on fasting glucose, insulin, HOMA-IR, triglycerides, LDL, or HDL. In women with reduced TIB, fasting glucose increased from early to late pregnancy whereas it decreased in women who had increased TIB (increased TIB: −5.0±3.2%, decreased TIB: 6.5±2.9%; $p=0.01$). Women with increased TIB tended to have smaller changes in fasting insulin (increased TIB:−1±25%, decreased TIB: 57±23%; $p=0.09$) and HOMA-IR (increased TIB: −6±28%, decreased TIB: 66±25%; $p=0.06$) compared to women who decreased TIB from early to late pregnancy (Figure 2a). As shown (Figure 2b), there were no significant changes in triglycerides, LDL, or HDL between women who had changes in sleep patterns across pregnancy. There were no differences in any measured cardiometabolic biomarkers between those who decreased TST and those who maintained TST ($p>0.05$).

Eating behaviors, energy intake, gestational weight gain

Compared to women who reduced TIB, women who increased TIB had a significantly lower energy intake across pregnancy (3078±103 vs 2538±128 kcals, $p=0.002$) and tended to have less gestational weight gain (466±59 vs 319±65 grams/week, $p=0.10$) (Figure 3). Women who increased TIB reported an increase in food cravings (23.8 ± 4.4% increase) compared to those who decreased TIB (5.07 ± 6.41% increase; $p=0.05$) or maintained a consistent TIB (7.2 ± 4.4% increase; $p=0.05$) across pregnancy. Despite changes to food cravings, TIB did not affect changes in diet quality as assessed by the Healthy Eating Index. Mindful eating, disinhibition, dietary restraint and perceived hunger from the eating inventory were not different between women with increased or decreased TIB across pregnancy.

There were no differences in daily energy intake or gestational weight gain between women with distinct changes in TST ($p=0.52$ and $p=0.27$, respectively).

Discussion

Reduced sleep and sleep disruption in pregnant women occur concurrently with declines in cardiometabolic health and in particular, glucose homeostasis (Facco, Grobman, et al., 2017;

Redfern et al., 2019). We hypothesized that the interaction between reduced sleep and the deterioration in cardiometabolic risk factors across pregnancy, may be in part due to changes in eating behavior that occur coincident with changes to sleep patterning. This observational cohort study in 52 pregnant women with obesity showed that sleep duration and quality (defined as sleep efficiency) assessed with actigraphy over 6 consecutive nights in early and late pregnancy, declined across pregnancy. In support of our hypothesis, compared to women with increased time in bed from early to late pregnancy, women with decreased time in bed had greater energy intakes and a worsened metabolic profile across pregnancy.

Sleep duration was short and sleep quality was poor and lower than previously reported in pregnant women without obesity (Tsai et al., 2016). Poor sleep quality across pregnancy has been associated with longer labor and an increased risk of cesarean delivery (Lee & Gay, 2004) but not with deterioration of cardiometabolic health markers (Facco, Grobman, et al., 2017). Given that pregnant women have poor sleep efficiency, it is not surprising that reduced sleep efficiency accompanies increased time spent in bed across pregnancy. Increased periods of nighttime wakefulness are possible due to both anatomical (e.g., postural changes for comfort or increased urinary frequency) and physiological (e.g., breathing disorders) adaptations with pregnancy. However, actigraphy without the use of a sleep diary is not able to discern if sleep efficiency is due to prolonged sleep onset, difficulty with waking in the morning, or increased awakenings throughout the night.

The wrist-worn actigraphy showed sleep duration and sleep quality declined from early to late pregnancy despite participants not reporting changes in sleep. Pregnant women poorly report sleep (Herring et al., 2013), and it is plausible that women in our study were not aware of the declines in sleep duration that they experienced. Thus, if we had only relied on validated self-reported instruments to quantify characteristics of sleep, we would have concluded that sleep did not impact changes in health outcomes across pregnancy. This underscores the necessity for studies to quantify sleep using objective instruments. Actigraphy is non-obtrusive and provides continuous, free-living sleep data that is not influenced by subject's unfamiliarity of a sleep laboratory. These benefits allow for sleep to be assessed over several nights without forcing standardized times for "lights-out" and "waking", customary of clinical sleep studies.

A major finding of our study was that glucose, insulin, and HOMA-IR change more favorably with longer time spent in bed across pregnancy. This provides novel evidence that sleep parameters, particularly time in bed, are integral to fully understand maternal hyperglycemia. It has been shown that for each 1 mmol/L increase in glucose with an oral glucose test during pregnancy, women have a 13% increased risk for the development of cardiovascular disease, even with glucose in the normal range (Retnakaran & Shah, 2019). For the fetus, exposure to increased maternal glycemia leads to increased glucose concentrations (Scholtens et al., 2019) and adiposity (Tint et al., 2020). Therefore, understanding the factors in pregnancy that can induce even subtle changes in maternal glucose could lead to improved outcomes for women and their infants.

Compared to women who maintained a consistent time in bed across pregnancy, those with shortened time in bed had a greater energy intake. The length of sleep obviously coincides

with the length of the overnight fast. We speculate that when sleep is shortened, higher energy intake may simply reflect a prolonged opportunity for eating. There is evidence supporting a link between the duration of eating throughout the day and glucose regulation. For example, limiting eating to only 8 hours of the day, and beginning in the morning (Sutton et al., 2018) has been identified as a strategy to improve metabolic regulation (Gabel et al., 2018). Although a 16-hour fast may not be feasible for all pregnant women, a recent study observed that each 1-hour increase in night fasting was associated with a 0.03 mmol/L decrease in fasting glucose during mid-pregnancy (Loy et al., 2017). Pregnant women could potentially benefit from restricting the daily eating window, however the feasibility and safety of such prescribed eating patterns has yet to be explored in pregnancy.

There are other factors which could influence both sleep and cardiometabolic health including physical activity, presence of sleep disordered breathing, and mental health. We have previously reported that physical activity levels (PAL) in this cohort were very low throughout pregnancy (Most et al., 2019; Most, Vallo, Gilmore, et al., 2018). Most women (88%) were considered sedentary (PAL<1.7), and thus physical activity unlikely contributes significantly to the decline in TIB. In the present study, we did not explicitly screen for obtrusive sleep apnea (OSA) nor was it an exclusion criterion. Given that the population comprised of pregnant women with obesity, it is not alarming 54% of the women were at high risk for sleep disordered breathing based off the Berlin Sleep Questionnaire (data not shown). Given that OSA is highly prevalent among women with obesity, we felt it was important to include these individuals within the analysis. While, sleep disordered breathing has been shown to negatively influence cardiometabolic risk (Drager, Togeiro, Polotsky, & Lorenzi-Filho, 2013), any awakenings caused by sleep disordered breathing would have been reflected in total sleep time. Maternal mood such as depression can also drastically influence both sleep and eating behaviors. We have previously shown the maternal depressive symptoms worsen as pregnancy progresses (Altazan et al., 2019). In the present study, maternal mood was assessed using the Beck Depression Index (BDI)-II during screening and late pregnancy, with no differences in early and late pregnancy between women who increased or decreased their TIB (data not shown).The relationship between sleep and eating may not be due to behavioral factors alone. A recent study described multiple shifts in a woman's chronotype throughout pregnancy and suggested that changes in clock genes within the brain may influence sleep timing (Martin-Fairey et al., 2019). A misalignment between sleep and eating can exacerbate chronodisruption and adversely impact normal metabolic control (Karlsson, Knutsson, & Lindahl, 2001). Thus, future studies should seek to understand the impact of pregnancy-induced chronotype shifts on changes to metabolic and cardiovascular health and birth outcomes.

Based on our finding that women with decreased time spent in bed had increased energy intake, it was not surprising that gestational weight gain also tended to be higher in this group. Gestational weight gain is an important indicator of pregnancy health and fewer than one-third of women gain appropriate weight throughout pregnancy (Deputy, Sharma, Kim, & Hinkle, 2015). Excess gestational weight gain increases risk for adverse pregnancy and delivery outcomes as well as postpartum weight retention (Muktabhant, Lawrie, Lumbiganon, & Laopaiboon, 2015). Thus, strategies to increase time spent in bed could be included in behavioral interventions to promote healthy gestational weight gain. It would be

important to add that while extension of time in bed could be a potential mechanism to promote healthy gestational weight gain, eating during any awakenings should be discouraged.

This study is strengthened by the objective and rigorous measurement of sleep over multiple consecutive nights at two time points in pregnancy with the use of actigraphy and a robust set of validated algorithms for use in sleep research. There are several analytical considerations associated with actigraphy which can influence outcomes and interpretation. The open source algorithms used to quantify sleep are based on bouts of inactivity defined as movement less than five degrees over 1) five minute or 2) ten minute intervals, during the sleep period time window. Importantly, these two bouts have been validated against polysomnography (van Hees et al., 2015). Analyzing actigraphy data using the five-minute inactivity bouts is proposed to have greater sensitivity in detecting sleep whereas the ten-minute inactivity bout may have greater sensitivity to detect wakefulness (van Hees et al., 2015). Given the extensive evidence that pregnant women are poor sleepers (Facco et al., 2010), we elected to define sleep using the five-minute bouts. It is possible that using the ten-minute inactivity bouts, which are more conservative, would result in a shorter TIB and TST and thereby potentially alter the interpretation of sleep changes on cardiometabolic health. Lastly, the algorithms used in the present analyses do not include daytime sleep or naps. However, it has been previously shown that daytime napping in pregnant women was not associated with actigraphy derived TST (Ebert, Wood, & Okun, 2015).

There is a limitation to our study design which should be considered by future research. First, the plasma samples were collected in the morning following an observed overnight sleep and standardized overnight fast on an inpatient unit. The sleeping period was controlled with “lights-out” and “lights-on”, and the timing and composition of the dinner meal was consistent for all subjects. Therefore, it is possible that the changes in circulating cardiometabolic markers we observed may have been artificially influenced results by acute changes to sleep and diet imposed by the study protocol. This design is consistent with most sleep studies and is considered rigorous for obtaining these measures. Future studies would benefit from collecting biological markers and eating behaviors in the morning following a habitual night of sleep where sleep and wake times are chosen by subjects. Future study designs could pair actigraphy to capture habitual sleep patterns with continuous glucose monitors for a closer evaluation of glucose regulation over the same time period.

In summary, this is the first analysis to demonstrate that a reduced time spent in bed throughout pregnancy worsens the metabolic phenotype during late pregnancy, and that an increase in energy intake is at least partially responsible for these adverse adaptations. Given the serious implications to both mother and offspring, it is crucial to understand any modifiable risk factors that further deteriorate cardiometabolic health during pregnancy. Studies in pregnant women that manipulate the eating window, independent of sleep are needed to fully understand the impact of changing sleep and eating patterns on cardiometabolic health during pregnancy.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Sleep quality and sleep duration decline across pregnancy in women with obesity
- Increased time in bed (TIB) across pregnancy improved glucose and insulin
- Increased TIB across pregnancy resulted in less energy intake
- Prolonged fast (TIB) may alter substrate availability; improving pregnancy health

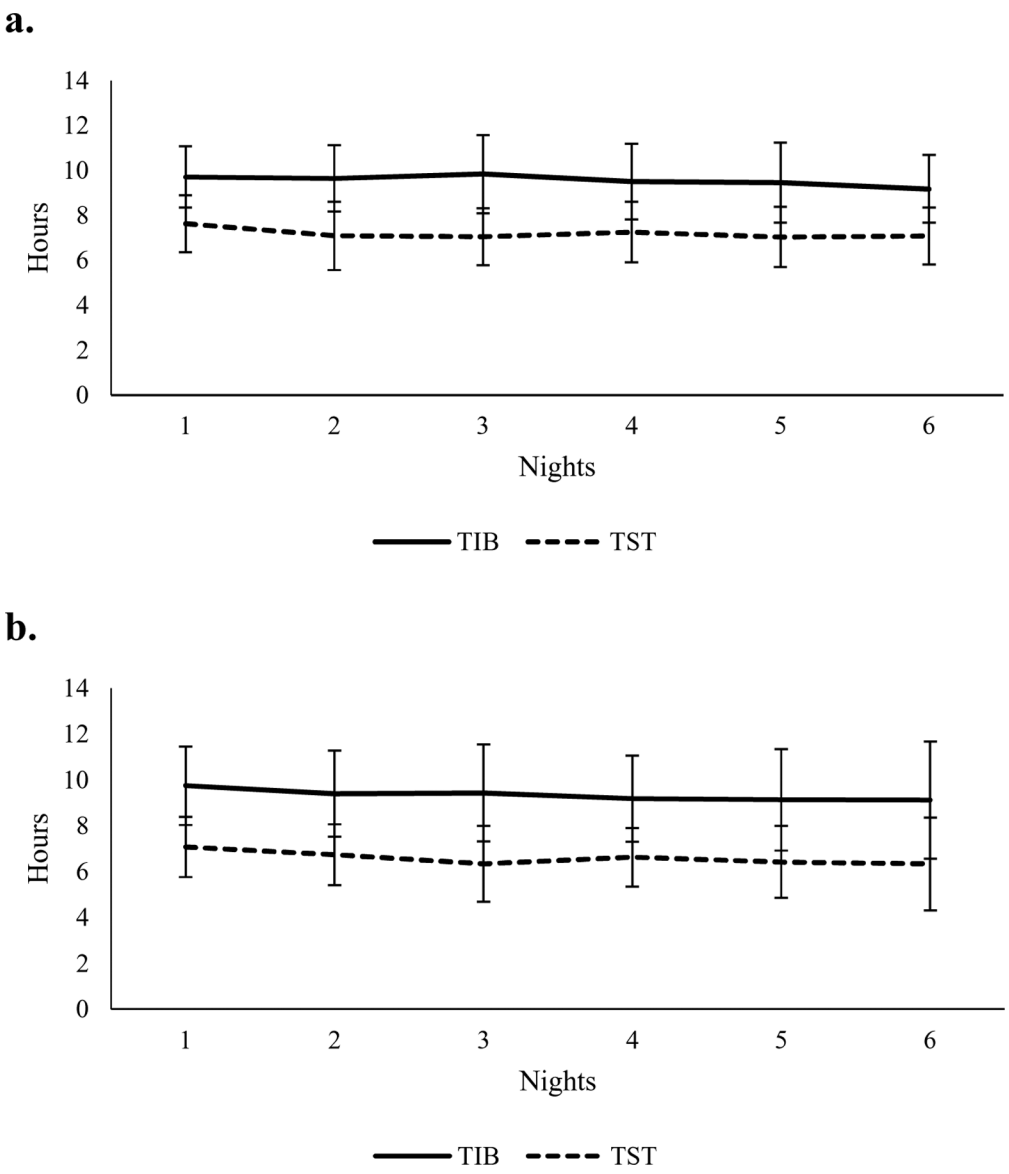

Figure 1. Patterns of time in bed (TIB) and total sleep time (TST) in early (a) and late (b) pregnancy.

Nightly sleep and night-to-night variability for time in bed (TIB) and total sleep time (TST). Data are presented as the mean ± standard deviation over six nights. Solid lines denote TIB and dashed lines denote TST.

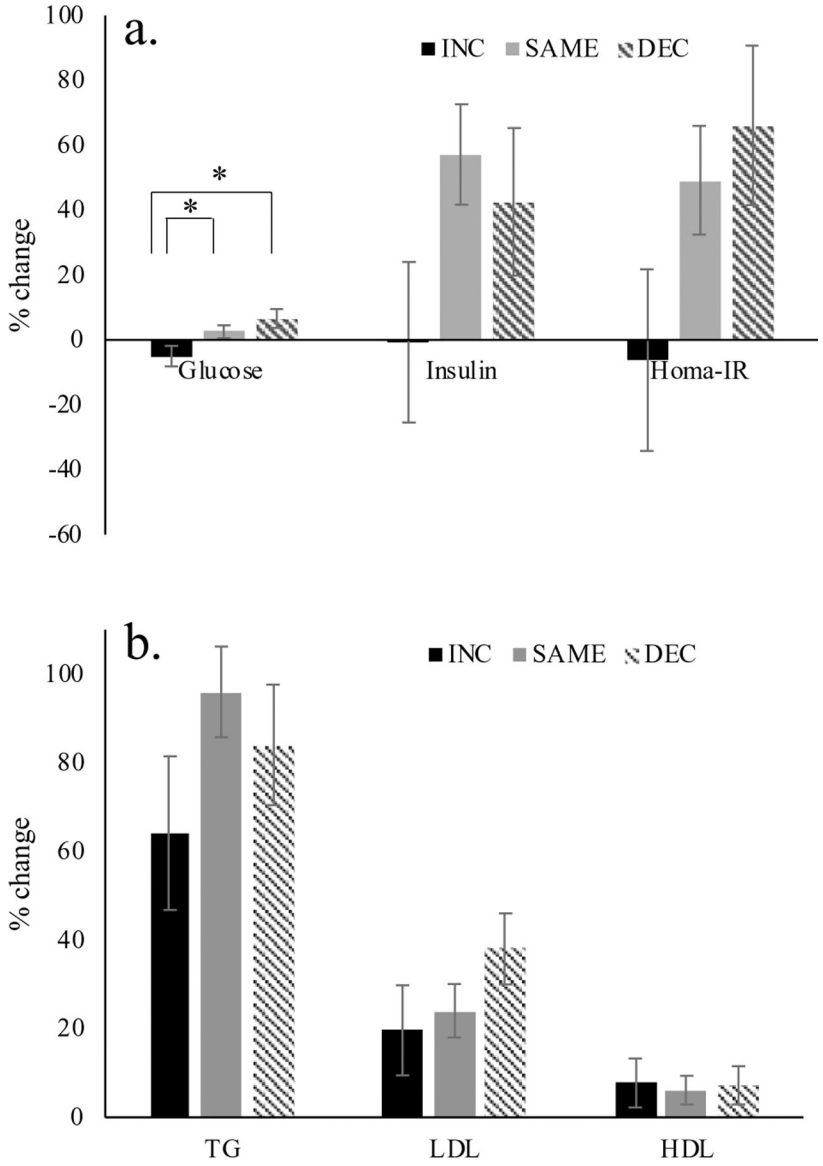

Figure 2. A comparison of changes in a) metabolic biomarkers and b) fasting lipids between women who increased (INC), decreased (DEC), or maintained (SAME) TIB from early to late pregnancy.

Percent changes in glucose, insulin, HOMA-IR, triglycerides (TG), and low and high-density lipoproteins (LDL, HDL) for increased, decreased, and no change in TIB from early to late pregnancy. Data are presented as the mean ± SEM and * denotes significant ($p < 0.05$) difference between groups. Means are adjusted for enrollment BMI. Black bars denote increased TIB, dashed bars denote decreased TIB, and grey bars denote no change from early to late pregnancy.

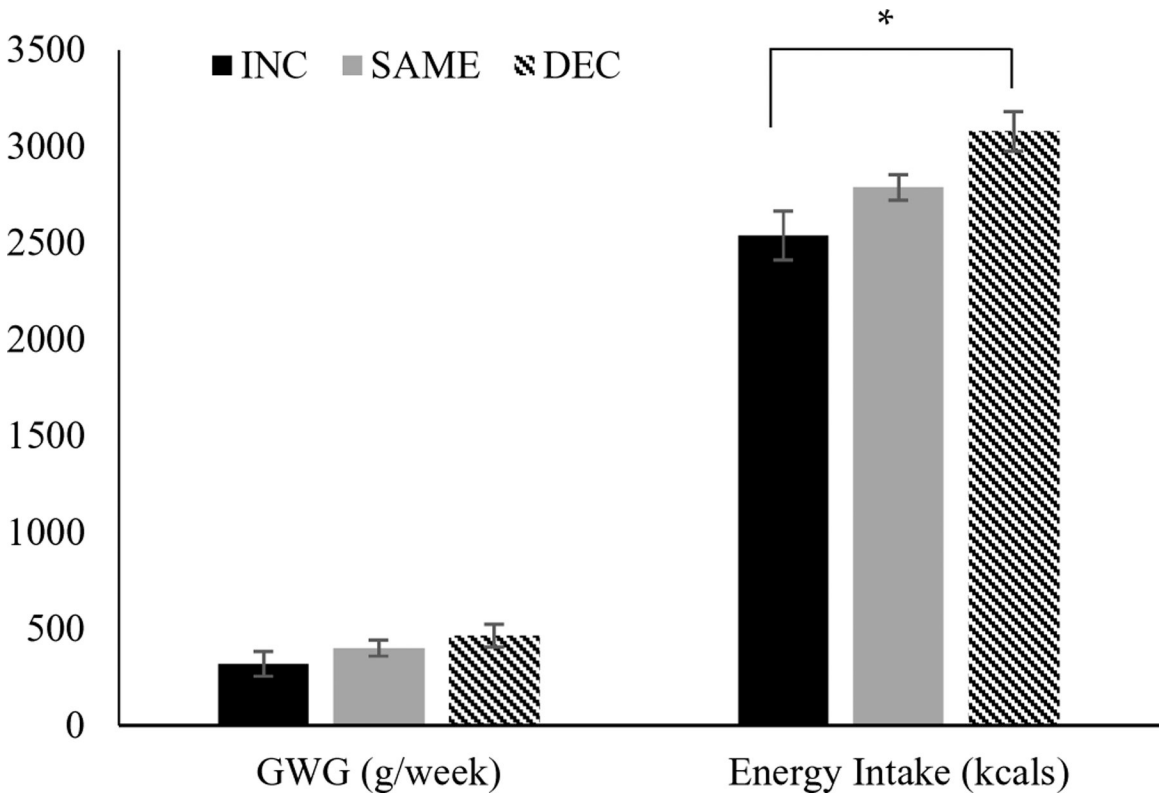

Figure 3. A comparison of changes in gestational weight gain (GWG) and energy intake between women who increased (INC), decreased (DEC), or maintained (SAME) TIB from early to late pregnancy.

Percent changes in gestational weight gain and energy intake for increased, decreased, and no change in TIB from early to late pregnancy. Gestational weight gain (GWG) is reported in grams per week of gestation and energy intake is reported in kilocalories (kcals) across pregnancy using the energy-intake method. Data are presented as the mean ± SEM and * denotes significant ($p < 0.05$) difference between groups. Means are adjusted for enrollment BMI. Black bars denote increased TIB, dashed bars denote decreased TIB, and grey bars denote no change from early to late pregnancy.

Table 1.

Objective and self-reported sleep in early and late pregnancy

Sleep Variable	Early	Late	*P*
Actigraphy			
Nightly sleep			
Time in bed (TIB, *h*)	9:24±0:08	9:14 ±0:08	0.236
Total sleep time (TST, *h*)	7:03±0:08	6:28±0:09	<0.001
Sleep efficiency (SE, *%*)	76±1	71±2	<0.001
Time of sleep onset (*h*)	22:02±0:18	22:09±0:23	0.754
Time of wake (*h*)	07: 41±0:13	7:30±0:18	0.719
Night-to-night variability (SD)			
Time in bed (TIB, *h*)	1:37±0:07	1:46±0:10	0.430
Total sleep time (TST, *h*)	1:16±0:06	1:19±0:06	0.704
Sleep efficiency (SE, *%*)	14±2	12±2	0.157
Time of sleep onset (*h*)	1:38±0:29	2:02 ±0:23	0.435
Time of wake (*h*)	1:58±0:26	2:23 ±0:34	0.565
Self-report			
Sleep duration on week nights/workdays (*h*)	7:17±0:11	7:17±0:13	0.962
Sleep duration weekend nights/off days (*h*)	8:15±0:15	8:30±0:14	0.307
Time to fall asleep (*minutes*)	26.06±3.76	27.81±4.15	0.694
Time spent awake at night (*minutes*)	25±4.0	30.72±4.4	0.109
Time of sleep onset on week nights/workdays (*h*)	21:56±0:24	22:17±0:17	0.481
Time of sleep onset on weekend nights/off days (*h*)	22:23±0:29	23:19±0:11	0.064
Time of wake on weekdays/workdays (*h*)	07:24±0:21	07:20±0:21	0.793
Time of wake on weekends/off days (*h*)	08:37±0:14	08:47±0:13	0.423
Epworth Sleepiness Scale (*score*)	8.83±0.52	8.73±0.54	0.849

Results are shown as mean and standard error of the mean (SEM) for early and late pregnancy. Actigraphy represents objective sleep measurement. Nightly sleep and night-to-night variability were measured with actigraphy and reflects the standard deviation (SD) of sleep measured over six nights. Self-reported sleep is captured through sleep questionnaires. All values are HH:MM, unless stated otherwise.