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Impact of change in bedtime variability on body composition and inflammation: Secondary findings from the Go Red for Women Strategically Focused Research Network

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Abstract

Variability in daily sleep patterns is an emerging factor linked to metabolic syndrome. However, whether reducing bedtime variability improves markers of disease risk has not been tested. Here, we assessed whether body composition and inflammation were impacted by changes in bedtime variability over a 6-wk period, during which, women were instructed to maintain healthy, habitual sleep patterns (one arm of a randomized trial). Data were available for 37 women (age 34.9±12.4 y, BMI 24.7±2.9 kg/m^2, sleep duration 7.58±0.49 h/night). Body composition and leukocyte platelet aggregates (LPA) were measured at baseline and endpoint using magnetic resonance imaging and flow cytometry, respectively. Sleep data were collected weekly using wrist actigraphy. Change in bedtime variability was calculated as the difference in the standard deviation of bedtimes measured during the 2-wk screening period and the 6-wk intervention period. Results showed that women who reduced their bedtime variability (n=29) during the intervention had reductions in total (P<0.001) and subcutaneous adipose tissue (P<0.001) relative to women who increased/maintained (n=8) bedtime variability. Similar effects were observed for LPA levels between women who reduced vs increased/maintained bedtime variability (P=0.011). Thus, reducing bedtime variability, without changing sleep duration, could improve cardiometabolic health by reducing adiposity and inflammation.

Short sleep duration and sleep disturbances are risk factors for obesity and cardiovascular disease (CVD)[1]. Night-to-night variability in sleep is an emerging risk factor for

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cardiometabolic diseases: in both cross-sectional and prospective analyses, variability in sleep onset timing was associated with over 25% higher odds of metabolic syndrome[2]. To elucidate mechanisms underlying this relation, we tested whether body composition was impacted by changes in bedtime variability. An additional aim was to assess changes in leukocyte platelet aggregates (LPA), given data linking these inflammatory markers to adiposity and cardiometabolic disorders[3–5]. We studied women participating in a clinical trial from the Go Red for Women Strategically Focused Research Network; the main purpose of the study was to test the effects of sleep duration, either adequate habitual sleep (HS) or reduced sleep, on cardiometabolic risk (Clinicalstrials.gov: NCT02835261).

Healthy women, age ≥ 20 y and BMI 20–33 kg/m^2, were screened over a 2-wk period using wrist actigraphy (Actigraph GT3X+, ActiLife LLC, Pensacola, FL) to ensure adequate sleep of 7–9 h/night. This validated device correlates well with polysomnography[6, 7]. In a crossover design, women maintained their HS or reduced their sleep by 1.5 h/night for 6 wk, with target bedtimes and waketimes provided for each phase. Sleep was continuously measured by actigraphy and reviewed on a weekly basis to ensure compliance with the sleep duration prescription. There was a 6-wk washout between phases. Only data from the HS phase were used for the present analyses. Body composition was measured using magnetic resonance imaging at baseline and 6 wk using a well-established protocol for whole-body assessments of adiposity[8]. Four repeated measurements by the same technician showed error ranges from 1.4% for skeletal muscle to 5.9% for intermuscular adipose tissue[9]. LPA were analyzed by whole-blood flow cytometry as previously described by our group[10, 11]. The study was approved by the Columbia University Irving Medical Center institutional review board; all women provided informed consent prior to their participation.

Standard deviations (SD) of nightly bedtimes were calculated for the screening period and the 6-wk HS phase. Data distribution for change in bedtime SD were skewed and bi-model. Therefore, women were dichotomized as those with increased or unchanged (subsequently referred to as 'increased') bedtime variability during HS relative to screening and those with decreased bedtime variability. Changes in body composition and LPA during the intervention were compared between groups using F-tests adjusted for total sleep duration. Results were considered significant at P<0.05.

No differences in baseline characteristics were observed between those who increased (n=8) vs those who decreased (n=29) their bedtime SD (Table). Sleep duration did not differ between screening and 6 wk HS intervention (−4.8±24.7min, P=0.24). Average percent change in bedtime SD was 24.4±25.2% in those who increased their bedtime variability and −39.9±23.5% in those who reduced their bedtime variability. Total and subcutaneous adipose tissue volumes decreased in women who reduced bedtime variability, while these values increased in women who increased bedtime variability (both P<0.001, Table). Changes in LPA mirrored those of adiposity; LPA levels decreased in women who reduced their bedtime variability and increased in those who increased their bedtime variability (P=0.011).

This is the first evidence that reducing sleep variability by stabilizing bedtimes can lead to reductions in adipose tissue. This outcome occurred in the context of sustained adequate

sleep duration and in the absence of any recommendation for weight management. These data suggest that methods to improve inter-night stability of sleep could improve body composition and reduce inflammation, thereby mitigating risk for the development of CVD.

Our results confirm associations of sleep variability with body composition from limited available studies[12, 13] but are also the first to demonstrate evidence towards causality. In older Japanese women, high night-to-night bedtime and sleep duration variability were associated with higher BMI, percent fat mass, and fat mass index, and lower percent lean mass and lean-to-fat mass ratio[12]. Papandreou et al.[13] further showed that weight loss success was related to sleep stability in participants of the PREDIMED-Plus weight loss intervention: those with greater sleep duration variability at baseline had smaller reductions in body weight 12-mo later, independent of sleep duration. By assessing changes in variability of sleep over time, we herein extend these findings by demonstrating that stabilizing bedtime reduces adiposity.

This study also provides novel insight into biological underpinnings of the relation between sleep variability and CVD risk. Previous work shows that LPA are inversely associated with BMI[14] and adiposity[5] in addition to experimental evidence of LPA reductions following bariatric surgery[5]. Our results thus suggest a potential pathway by which reductions in sleep variability exert effects on endothelial inflammation via reductions in adiposity. Clinical trials designed specifically to isolate the acute and long-term effects of experimental manipulations to nightly bedtime patterns on adiposity and inflammatory markers are needed to confirm this speculation and elucidate the causal pathway between bedtime variability and CVD risk. Furthermore, those studies should address whether effects differ by characteristics such as weight status, sex, or race/ethnicity.

The clinical trial from which these data were gathered was not designed to test the impact of bedtime stability on body composition; therefore, our results should be considered exploratory. However, our data are robust, with at least 2 wk of objectively-measured sleep during free-living status in addition to 6 wk of daily measurements of sleep, also using actigraphy, during an intervention period that aimed to stabilize sleep duration. This same method has been used to determine variability in sleeping behaviors[12]. Furthermore, bedtime variability was changed in the context of maintenance of adequate sleep duration. It is unknown from this study whether maintaining stable bedtimes in the context of insufficient sleep would have similar ramifications for weight management.

Our results provide novel preliminary information showing that reducing bedtime variability can improve body composition and reduce inflammation over time. Given that bedtimes are readily modifiable, this may provide an easy public health message to maintain healthy sleep hygiene, particularly stable bedtime routine, to achieve better weight management and reduced CVD risk.

Sources of funding:

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Table.

Data summarized as mean ± SD or count (%).

Variable	Increased/same bedtime variability (N=128)	Reduced bedtime variability (N=29)	P-value[*]
Age, y	36.9 ± 15.0	34.4 ± 11.8	0.621
Race			0.663
White	5 (63)	14 (48)	
Other	3 (37)	15 (52)	
Baseline weight, kg	62.2 ± 5.0	66.5 ± 7.8	0.153
Baseline BMI, kg/m^2	23.5 ± 2.1	25.1 ± 3.0	0.190
Baseline sleep duration, min	453.3 ± 29.3	455.2 ± 30.2	0.875
Baseline bedtime	12:00 AM	10:48 PM	0.109
Baseline bedtime SD, min	49.7 ± 9.5	57.2 ± 27.4	0.218
Weight change, kg	0.48 ± 1.19	−0.66 ± 1.37	0.059
TAT change, L[†]	0.63 ± 0.41	−0.52 ± 0.98	<0.001
VAT change, L	0.05 ± 0.17	−0.03 ± 0.10	0.297
SAT change, L	0.56 ± 0.31	−0.48 ± 0.86	<0.001
WBV no lungs change, L	0.23 ± 0.91	−0.75 ± 0.90	0.016
IMAT change, L	0.03 ± 0.03	−0.01 ± 0.12	0.134
SM change, L	−0.08 ± 0.49	−0.19 ± 0.47	0.602
Leukocyte platelet aggregates, %[‡]	8.42 ± 16.59	−8.42 ± 10.82	0.011

Abbreviations: BMI, body mass index; IMAT, intermuscular adipose tissue; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; WBV, whole-body volume.

[*] Based on either the two-sample t-test or the chi-squared test.

[†] To convert L of adipose tissue to kg, multiply by 0.9 kg/L. To convert L of muscle to kg, multiply by 1.1 kg/L[15].

[‡] Data are available for n=6 women in the group that did not change/increased bedtime variability and n=18 women in the group that decreased bedtime variability. Leukocyte platelet aggregates are percentage of leukocytes positive for adherent platelets.