HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2020 February 01.

Published in final edited form as:

J Pediatr. 2019 February ; 205: 257–264.e1. doi:10.1016/j.jpeds.2018.10.027.

Too Late and Not Enough: School Year Sleep Duration, Timing, and Circadian Misalignment Are Associated with Reduced Insulin Sensitivity in Adolescents with Overweight/Obesity

Stacey L. Simon, PhD[1], **Cecilia Diniz Behn, PhD**[2,3], **Melanie Cree-Green, MD, PhD**[3,7], **Jill L. Kaar, PhD**[3], **Laura Pyle, PhD**[4], **Stephen M. M. Hawkins**[1], **Haseeb Rahat, BS**[3], **Yesenia Garcia-Reyes, MS**[3], **Kenneth P. Wright Jr., PhD**[5,6], and **Kristen J. Nadeau, MD, MS**[3,7]

[1]Division of Pulmonary Medicine, Department of Pediatrics, University of Colorado Anschutz Medical Campus & Children's Hospital Colorado, Aurora, CO

[2]Department of Applied Mathematics and Statistics, Colorado School of Mines, Golden, CO

[3]Division of Endocrinology, Department of Pediatrics, University of Colorado Anschutz Medical Campus & Children's Hospital Colorado, Aurora, CO

[4]Department of Pediatrics, University of Colorado Anschutz Medical Campus & Children's Hospital Colorado, Aurora, CO

[5]Sleep & Chronobiology Laboratory, Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO

[6]Division of Endocrinology, Metabolism, and Diabetes, University of Colorado Anschutz Medical Campus, Aurora, CO

[7]Center for Women's Health Research, University of Colorado Anschutz Medical Campus, Aurora, CO

Abstract

Objectives—To examine the relationship between insulin resistance (IR) and sleep/circadian health in overweight/obese adolescents. We hypothesized that insufficient and delayed sleep would be associated with IR in this population.

Study design—Thirty-one adolescents (16.0±1.4y, 77% female) with BMI ≥90 percentile for age/sex were recruited from outpatient clinics at a children's hospital. Participants underwent one week of objective home sleep monitoring with wrist actigraphy during the academic year. A 3-h oral glucose tolerance test was conducted, followed by in-laboratory salivary dim light melatonin

Corresponding Author: Stacey L. Simon, 13123 East 16th Avenue Box B395, Aurora, CO 80045, Phone: 720-777-5681; Fax: 720-777-7201; Stacey.Simon@childrenscolorado.org.

Data Statement

Data sharing statement available at www.jpeds.com.

Portions of this study were presented at the SLEEP annual meeting, June 2–6, 2018, Baltimore, Maryland.

sampling every 30–60m from 5pm to noon the following day. Regression analyses between sleep and circadian variables with IR were examined.

Results—Longer sleep time and time in bed on weekends and weekdays, and earlier weekday bedtime were significantly associated with better insulin sensitivity. Participants who obtained less than the median duration of sleep per night (6.6h) had evidence of IR with compensatory insulin secretion compared with those obtaining ≥6.6h. Wider phase angle between bedtime and melatonin onset, indicating a later circadian timing of sleep onset, was significantly associated with IR.

Conclusions—Short sleep duration, later weekday bedtime, and later circadian timing of sleep were associated with IR in a cohort of adolescents with overweight/obesity during the school year. Further research is needed to better understand the physiology underlying these observations, and evaluate the impact of improved sleep and circadian health on metabolic health in this at-risk population.

Keywords

Circadian rhythm; sleep restriction; insulin resistance; pediatrics

Overweight/obesity currently affects ~33% of adolescents in the United States.[1] Rates of related comorbidities such as type 2 diabetes (T2D) are also rising in teens and present more aggressively, with rapid onset of β-cell failure in youth compared with adults.[2–4] Insulin resistance (IR) is a significant risk factor for T2D and adolescents with overweight/obesity are at particular risk. Insulin sensitivity (S_i) decreases by approximately 50% in all adolescents during puberty, and over half of teens with overweight/obesity also demonstrate further IR relative to their pubertal-matched lean peers[5–8]. Weight-management interventions tend to be less effective for adolescents[9], calling for alternative prevention and intervention targets for overweight/obesity and T2D in youth to prevent future morbidity and mortality.

Concurrent with the rise in overweight/obesity and pubertal effects on S_i, adolescents are at increased risk for poor sleep and circadian health. A physiological delay in circadian rhythms, coupled with increased academic and social demands, greater electronics use, and early school start times, result in high rates of insufficient sleep in adolescence[10–12]. Up to 25% of adolescents obtain <6 h of sleep per night, well below the 8–10 hours recommended for this age group[13–16]. Evidence in adults that poor sleep and circadian health results in abnormal glucose metabolism suggests that sleep problems may be a target for intervention. Specifically, prior studies in adults have demonstrated relationships between sleep measures and S_i. Habitually short-sleeping adults as well as those undergoing experimentally-induced sleep restriction demonstrated reduced S_i[17–21].

Few studies examining the relationship between sleep duration and timing with insulin sensitivity have been performed in adolescents. Some studies found results comparable with adults with shorter sleep duration in adolescents correlating with lower S_i[22, 23], whereas another found that this relationship was attenuated after controlling for adiposity[24].

Adolescent boys had reduced S_i after 3 nights of sleep restriction (4h per night) compared with 3 nights of extended sleep (9h per night)[25].

The goal of this study was to examine the relationship between S_i and sleep/circadian health, including duration and timing of sleep, and melatonin timing in adolescents with overweight/obesity. We hypothesized that adolescents with short sleep duration, later sleep timing, and later circadian timing would have worse S_i.

Methods

Participants were recruited from adolescent medicine and weight-management specialty clinics at Children's Hospital Colorado between September, 2014 and May, 2017 and enrolled in one of 2 protocols with identical measures except where noted below (APPLE cohort NCT02157974 and CIRC cohort NCT02585830). All participants were between the ages of 14–19 years and attending high school, with BMI ≥90%ile for age and sex and were habitually sedentary (<3 hours of physical activity per week). To minimize the varied effects of puberty on IR, all participants were in late puberty, defined as Tanner puberty stage 4 or 5. Exclusion criteria included diabetes ($HbA_1c \geq 6.5\%$), anemia, prior diagnosis of obstructive sleep apnea (CIRC cohort only) and medications impacting IR or sleep. All procedures were approved by the Colorado Clinical and Translational Sciences Institute Scientific Advisory Committee and the Colorado Multiple Institutional Review Board. All youth and their parents provided appropriate informed assent and/or consent prior to participation.

Procedures

After a screening visit with a physical examination and laboratory tests (ie, HbA_1C,) to evaluate inclusion/exclusion criteria, participants were given a wrist actigraphy monitor to wear for seven days at home prior to an outpatient study visit. Fasting laboratory tests were obtained and a 3-hour oral glucose tolerance test (OGTT) was performed to assess S_i. Participants were admitted to the Children's Hospital Colorado Clinical and Translational Research Center (CTRC) at 4pm and entered dim light conditions (<5 lux measured at angle of gaze) for the duration of the stay. Salivary melatonin samples were obtained every 30–60 minutes from 5pm to noon the following day. Participants from the APPLE cohort (N = 11) had only hourly-sampled evening and morning melatonin available. All studies were performed on Thursday or Friday to be consistent with the amount of accumulated sleep debt incurred over the week. Participants were scheduled in the follicular phase when possible, as menstrual timing can influence measures of S_i, sleep, circadian rhythms, and melatonin levels[26]. Participants were also asked to refrain from exercising in the 72 hours prior to study, as activity can affect S_i.

Measures

Sleep/wake: Participants wore a Spectrum Plus actigraphy monitor (Phillips Respironics, Bend, OR), a watch-like device that estimates sleep duration and timing, on their non-dominant wrist for 7 days at home prior to their study visits. Participants completed a concurrent sleep diary reporting their bedtimes and waketimes and sleep start and wake

times were manually selected to facilitate accurate scoring of sleep/wake episodes[27]. Total sleep duration, sleep onset latency, mid-sleep time (sleep midpoint), number of awakenings, wake after sleep onset (WASO), and sleep efficiency were calculated using Actiware Sleep v6 software and standard scoring rules and a medium sensitivity (Phillips Respironics, Pittsburgh, PA)[27].

Dim light melatonin onset and offset: Saliva (~1mL) was collected in 30–60 minute intervals in dim light (<5 lux in the angle of gaze, approximately the light level of candlelight or civil twilight; EasyView Light Meter, Extech Instruments, Boston, MA) from approximately 5pm until noon the following day. Participants were instructed to remain seated/lying (to avoid impact of position on melatonin levels) and eating and drinking was not permitted for 15 minutes prior to sampling to prevent sample contamination. Samples were centrifuged for 10 minutes at 3500 RMP and 4 ° C before transfer via pipette and then frozen at −80 ° C. Melatonin onset (DLMOn) was defined as the linear interpolated clock time at which evening salivary melatonin concentrations increased and remained above a 3pg/mL threshold. Melatonin offset (DLMOff) was the linear interpolated clock time at which salivary melatonin concentrations fell below this threshold. Later DLMOn and DLMOff are indicative of a later circadian rhythm[28]. Phase angles of entrainment, a quantification of the temporal alignment between actual sleep behaviors with the internal circadian clock, were computed as the time interval between each circadian marker (DLMOn and DLMOff) and actigraphic estimates of sleep (bedtime and wake time)[28].

Insulin sensitivity: After an overnight fast, participants completed an OGTT in the morning. Participants consumed a 75-gram dextrose drink (76–78 grams in the APPLE cohort) and serum for glucose and insulin concentrations were collected at baseline and every 30 minutes for three hours. A fasting lipid panel was also drawn at baseline. The Matsuda Index, calculated as 10,000/[[fasting insulin (μU/ml) × fasting glucose (mmol/l)] × [mean OGTT insulin (μU/ml) × mean OGTT glucose (mmol/l)]], was used to estimate S_i[29]. The Matsuda index correlates strongly with the more invasive hyperinsulinemic-euglycemic clamp and has been validated in many different populations and disease conditions[29]. HOMA-IR (homeostatic model assessment; [fasting insulin (μU/ml) × fasting glucose (mmol/l)] / 22.5)[30] was also calculated. Additionally, the mean and area under the curve (AUC) for insulin and glucose concentrations during the entire OGTT were estimated using the trapezoidal method[31].

Sleep-disordered breathing screening: The Sleep Disturbances Scale for Children (SDSC[32]) was completed by the CIRC cohort only to assess for symptoms of common sleep disorders over the past 6 months. Items are summed and raw scores are converted to t-scores for each subscale; the Sleep Breathing Disorders subscale was used in analyses. The measure has demonstrated adequate internal consistency (Cronbach alpha = 0.71–0.79)[32]. The APPLE cohort had in-laboratory overnight polysomnography during their overnight study visit.

Laboratory Assays:

Analyses were performed by the University of Colorado Anschutz Research core laboratory or the Children's Hospital Colorado clinical laboratory except where noted. Triglycerides and HDL were analyzed enzymatically (Hitachi 917 autoanalyzer; Boehringer Mannheim Diagnostics, Indianapolis, IN). DCCT-calibrated high performance ion-exchange liquid chromatography was used for HbA1c (Bio-Rad Laboratories, Hercules, Calif). Radioimmunoassay was used to analyze serum insulin (Millipore, Billerica, MA). Melatonin was assayed using radioimmunoassay (Buhlmann Laboratories AG, Schonenbuch, Switzerland) at the Sleep and Chronobiology Laboratory at the University of Colorado Boulder.

Statistical Analyses

Descriptive statistics reported are: mean and SD for normally-distributed variables or median and min-max for non-normally-distributed variables. Sleep midpoint was calculated as: time in bed + [(time out of bed – time in bed)/2] and social jetlag was calculated as the difference between weekend and weekday sleep midpoints. Linear regression analyses were calculated to examine the association of continuous sleep variables with S_i variables. Independent samples t-tests examined differences in S_i variables for youth obtaining greater than vs less than the median sleep duration on weekday nights for the sample (6.6 hours). Statistical software (SAS 9.0 and SPSS Statistics 24) were utilized for analyses.

Results

A total of 31 participants met inclusion and exclusion criteria. Average age was 16.0 ± 1.4 years and the majority were female (77.4%); 58% were Hispanic, 26% African-American and 16% Caucasian. Average BMI percentile was 96.9 ± 2.4, and all participants were in late puberty with either Tanner stage 4 (29%) or 5 (71%). Mean S_i as assessed by Matsuda Index was 4.1 ± 2.2 and by HOMA-IR was 3.0 mg/dl ± 1.8. Table 1 (available at www.jpeds.com) lists all participant characteristics.

The overall cohort obtained insufficient sleep on both weekend and weekday nights (average total sleep time = 7.5 ± 0.88 h and 6.6 ± 0.96 h, respectively) compared with the recommended 8–10 hours for this age group[16]. Sleep duration and time in bed were significantly longer, and sleep timing (bedtime, wake time, and midpoint time) were significantly later on weekend nights compared with weekdays. Table II shows actigraphy and melatonin data. Participants who obtained less than the median duration of sleep on weekdays had significantly wider phase angles between DLMOff and wake time ($P = .04$), indicating more time between melatonin offset and waketime, and more narrow phase angles between DLMOn and wake time ($p = 0.02$), indicating less time between melatonin onset and waketime, compared with those obtaining more than the median sleep duration on weekdays.

The average Sleep Breathing Disorders score from the SDSC was 53.8 ± 9.6. This score was not significantly correlated with any demographic, insulin sensitivity, or sleep/circadian variable so was not controlled for in subsequent analyses. Of the participants with

polysomnography, mean apnea-hypopnea index was 1.9 events/hour and only 1 participant had an AHI >5. Analyses were re-run excluding this participant and results did not change.

Actigraphy and Insulin Sensitivity

Our analyses identified associations between several actigraphy-derived measures and S_i. Regression analyses between actigraphy and S_i variables for the cohort revealed that longer total sleep time and more time in bed on both weekend and weekdays, and earlier weekday bedtime were significantly associated with better S_i (Figure 1). Social jetlag (the discrepancy between sleep on school days and weekend days) was not significantly associated with S_i.

Comparing participants who obtained <6.6 hours of sleep per night with those who obtained ≥6.6 h per night revealed significant differences between groups for Matsuda Index ($t(26) = =2.9$, $p = 0.007$) and HOMA-IR ($t(27) = 2.4$, $p = 0.02$), with participants obtaining ≥6.6 h sleep having better S_i. Additionally, a significant difference was found between groups for AUC for insulin ($p = 0.03$), but not AUC glucose ($p = 0.2$), with participants obtaining ≥6.6 h sleep having a lower insulin AUC (Figure 2).

Melatonin and Insulin Sensitivity

Regression analyses between melatonin and S_i variables show that shorter phase angles between weekday bedtime and DLMOn, indicating sleep onset at an earlier circadian time, were significantly associated with better S_i (HOMA: beta = 0.44, SE = 0.34, $p = 0.03$). Greater phase angles between weekday bedtime and DLMOff were also significantly associated with better S_i (Matsuda: beta = 0.46, SE = 0.38, $p = 0.019$; HOMA: beta = −0.65, SE = 0.27, $p < 0.001$) and reflect longer sleep duration during the biological night. Regression analyses between DLMOn, DLMOff, and waketime phase angles were not significant ($p > 0.05$) (Figure 3).

Discussion

In our sample of adolescents with overweight/obesity during the academic year, we found significant associations between sleep and circadian variables with S_i. Specifically, participants obtaining more sleep, spending more time in bed on both weekends and weekdays, and having earlier weekday bedtimes had better S_i. Going to sleep at a later circadian time was associated with worse S_i. These findings confirm our hypotheses and are consistent with the extant adult literature. Moreover, this study adds to the pediatric literature by examining objectively measured sleep and circadian rhythm in adolescents with overweight/obesity in the home environment with strict controls to minimize influences on S_i (eg, physical activity, weight status, menstrual cycle).

Typical imposed early school start times coupled with the “eveningness” tendency of adolescence limit teens’ ability to sleep longer and contribute to insufficient sleep duration. Indeed, our cohort had a school night sleep duration that was on average ~1.5 hours below the minimum number of hours of sleep recommended for adolescents. Moreover, short sleep duration was significantly associated with impaired S_i in our cohort. Other studies using community samples of both healthy teens and obese youth have also found that short sleep duration is associated with reduced S_i in adolescents[22, 23, 25, 33], with some studies also

demonstrating that long sleep duration is associated with impaired glucose homeostasis, suggesting a "u-shaped" relationship between sleep duration and S_i[24, 34]. In contrast, a large clinical sample of obese adolescents failed to find a relationship between sleep duration and metabolic measures[35]. However, these studies have limitations in their sleep assessment methodology including examining sleep based on self-report, considering only a single night of polysomnography, or imposing laboratory-based sleep restriction paradigms not typical of adolescent's sleep in a school week. Our sleep data, recorded over a full week in the home setting, confirms that sleep duration was salient with regards to S_i in adolescents with overweight/obesity. Further, we controlled for many confounding variables such as physical activity, weight status, and menstrual cycle, and performed metabolic studies at the end of a school week which may have enhanced our ability to detect associations between sleep/circadian health and S_i.

Our finding that later weekday bedtimes, especially bedtimes occurring later with respect to DLMOn, are associated with reduced S_i is alarming given that adolescents have an increased propensity for a delayed sleep phase and eveningness preference. In a sample of pre-adolescents (ages 10–13 years), late estimated chronotype as assessed by sleep midpoint on free days and self-report questionnaire was correlated with higher fasting plasma glucose independent of weight status[36]. Late chronotype has been associated with metabolic disorders and increased morbidity in adults[37]. Furthermore, shift work in adults has been associated with increased risk of metabolic disorders[38], and experimentally induced circadian misalignment (imposed wakefulness occurring during the biological night) in a sample of adults resulted in lower Si[39]. These metabolic effects are hypothesized to be caused, in part, due to a mismatch between circadian rhythm and sleep timing.[38] Although the relationship between phase angle of waketime and melatonin offset was not significantly associated with S_i, this may reflect the reduced level of control that teens have over waketime compared with bedtime during the academic year. This study utilized objective measurement of circadian rhythm with salivary melatonin assessment to investigate associations with S_i in this population. Further research on the effects of sleep and circadian timing on S_i is needed in adolescents to determine whether common societal challenges to sleep, such as early school start times, may adversely impact the cardiometabolic health of adolescents.

Sleep duration, timing, and melatonin variables for participants in the current sample were similar to the study by Crowley et al of 13–16 year-olds during the school year[40]. We found significant differences in actigraphy variables between sleep on weekdays and weekends in our cohort. Increased duration of sleep on weekends suggests that adolescents may be trying to compensate for weekday sleep restriction. Later timing of sleep on weekends is consistent with the increased propensity for a delayed sleep phase and eveningness preference reported in adolescents and extended recovery sleep. However, this change in sleep timing also indicates that our cohort may be experiencing weekend phase delay or social jet lag that is common in adolescents and contributes to circadian misalignment and may impact subsequent mood and cognitive function[28, 41, 42].

S_i in our study was measured by OGTT. Among our normal glycemic adolescent cohort, participants who obtained <6.6 hours of sleep per night had significantly greater insulin

AUC, indicating IR. This is concerning as IR is a risk factor for T2D and progression to diabetes occurs more rapidly in teens than in adults[2, 43]. Future work to explore the physiological mechanisms involved in the relationship between sleep and circadian health and insulin response is urgently needed and may inform novel prevention and intervention strategies for IR and T2D for adolescents.

Strengths of our study include circadian phase assessment using full-night salivary melatonin sampling in dim light conditions, objective measurement of sleep for multiple nights in the home environment (actigraphy), and use of an OGTT which builds upon previous research that focused only on sleep but not circadian health and relied primarily on fasting measures of S_i. Additionally, the study design minimized confounders by controlling for the effects of both chronic and acute exercise, pubertal and weight status, menstrual cycle, and day of study visit on S_i. However, the study was limited by several factors including relatively small sample size and cross-sectional study design. Additional study in a larger and more diverse sample is needed. Moreover, although the CIRC study excluded participants with a diagnosis of OSA and screened for sleep disorder symptoms, future study using polysomnography to objectively assess for sleep-disordered breathing and to examine sleep staging is recommended.

Suggestions for future research include use of more rigorous stimulated measures of S_i or insulin secretion such as intravenous glucose tolerance test (IVGTT) or the gold-standard hyperinsulinemic-euglycemic clamp to verify and expand upon these findings. Experimental designs to manipulate sleep and circadian rhythms may help elucidate causal mechanisms underlying the relationship between sleep and circadian timing with S_i in adolescents.

In conclusion, we found that short and late sleep and later circadian timing of sleep were associated with reduced S_i in a cohort of adolescents with overweight/obesity during the school year. Clinicians should consider assessment and treatment of sleep and circadian health, including sleep duration, time in bed, and sleep timing, when working with adolescents with overweight/obesity. Further research is needed to better understand the physiology behind these observations, as well as to evaluate sleep and circadian interventions or delayed school day start times as recommended by the American Academy of Pediatrics[44] as a possible means for improving metabolic health for this population.

Acknowledgments:

We would thank the participants and their families for taking part in our research and our CTRC nursing staff for their assistance in performing these studies.

Supported by the following grants: SLS: UCD Center for Women's Health Research Pilot Award; SLS & CDB: Children's Hospital Colorado & Colorado School of Mines Collaborative Pilot Award; MCG: K12HD057022; K23DK107871; Doris Duke Foundation Caregivers Fellowship 2015212; Boettcher Webb-Waring Biomedical Research Award; Colorado CTSA: UL1TR002535. The funding sources had no involvement in study design, collection, analysis, and interpretation of data, the writing of this report, or the decision to submit the paper for publication. C.B. receives research support from Jazz Pharmaceuticals. K.W. receives research support from Philips Inc, CurAegis Technologies (formerly known as Torvec Inc), and Somalogics; has served as a paid consultant or as a paid member of scientific advisory boards for the Sleep Disorders Research Advisory Board - National Heart, Lung and Blood Institute, CurAegis Technologies, Circadian Therapeutics, LTD; and has received speaker/educational consultant honorarium fees from the American Academy of Sleep Medicine, American College of Chest Physicians, American College of Sports Medicine, American Diabetes Association, Associated Professional Sleep Societies, and the Obesity Medicine Association. The other authors declare no conflicts of interest.

List of Abbreviations:

AUC	area under the curve
DLMOn	dim light melatonin onset
DLMOff	dim light melatonin offset
HOMA-IR	homeostatic model assessment
IR	insulin resistance
OGTT	oral glucose tolerance test
T2D	type 2 diabetes
WASO	wake after sleep onset

References

[1]. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011–2012. Jama. 2014;311:806–14. [PubMed: 24570244]

[2]. Copeland KC, Zeitler P, Geffner M, Guandalini C, Higgins J, Hirst K, et al. Characteristics of adolescents and youth with recent-onset type 2 diabetes: the TODAY cohort at baseline. The Journal of clinical endocrinology and metabolism. 2011;96:159–67. [PubMed: 20962021]

[3]. Zeitler P, Hirst K, Pyle L, Linder B, Copeland K, Arslanian S, et al. A clinical trial to maintain glycemic control in youth with type 2 diabetes. The New England journal of medicine. 2012;366:2247–56. [PubMed: 22540912]

[4]. Dabelea D, Mayer-Davis EJ, Saydah S, Imperatore G, Linder B, Divers J, et al. Prevalence of type 1 and type 2 diabetes among children and adolescents from 2001 to 2009. Jama. 2014;311:1778–86. [PubMed: 24794371]

[5]. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes care. 1991;14:173–94. [PubMed: 2044434]

[6]. Shaw J Epidemiology of childhood type 2 diabetes and obesity. Pediatric diabetes. 2007;8 Suppl 9:7–15. [PubMed: 17991128]

[7]. Lee JM, Okumura MJ, Davis MM, Herman WH, Gurney JG. Prevalence and determinants of insulin resistance among U.S. adolescents: a population-based study. Diabetes Care. 2006;29:2427–32. [PubMed: 17065679]

[8]. Cree-Green M, Triolo TM, Nadeau KJ. Etiology of insulin resistance in youth with type 2 diabetes. Current diabetes reports. 2013;13:81–8. [PubMed: 23135953]

[9]. Steele RG, Aylward BS, Jensen CD, Cushing CC, Davis AM, Bovaird JA. Comparison of a family-based group intervention for youths with obesity to a brief individual family intervention: a practical clinical trial of positively fit. Journal of pediatric psychology. 2012;37:53–63. [PubMed: 21852343]

[10]. Carskadon MA, Vieira C, Acebo C. Association between puberty and delayed phase preference. Sleep. 1993;16:258–62. [PubMed: 8506460]

[11]. Carskadon MA, Wolfson AR, Acebo C, Tzischinsky O, Seifer R. Adolescent sleep patterns, circadian timing, and sleepiness at a transition to early school days. Sleep. 1998;21:871–81. [PubMed: 9871949]

[12]. Crowley SJ, Acebo C, Carskadon MA. Sleep, circadian rhythms, and delayed phase in adolescence. Sleep medicine. 2007;8:602–12. [PubMed: 17383934]

[13]. Smaldone A, Honig JC, Byrne MW. Sleepless in America: inadequate sleep and relationships to health and well-being of our nation's children. Pediatrics. 2007;119 Suppl 1:S29–37. [PubMed: 17272582]

[14]. National Sleep Foundation. Sleep in America Poll: Teens and Sleep. Washington, DC: National Sleep Foundation; 2006.

[15]. Bartel KA, Gradisar M, Williamson P. Protective and risk factors for adolescent sleep: a meta-analytic review. Sleep medicine reviews. 2015;21:72–85. [PubMed: 25444442]

[16]. Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, et al. Recommended Amount of Sleep for Pediatric Populations: A Consensus Statement of the American Academy of Sleep Medicine. Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine. 2016;12:785–6. [PubMed: 27250809]

[17]. Broussard JL, Ehrmann DA, Van Cauter E, Tasali E, Brady MJ. Impaired insulin signaling in human adipocytes after experimental sleep restriction: a randomized, crossover study. Annals of internal medicine. 2012;157:549–57. [PubMed: 23070488]

[18]. Buxton OM, Pavlova M, Reid EW, Wang W, Simonson DC, Adler GK. Sleep restriction for 1 week reduces insulin sensitivity in healthy men. Diabetes. 2010;59:2126–33. [PubMed: 20585000]

[19]. Darukhanavala A, Booth JN, 3rd, Bromley L, Whitmore H, Imperial J, Penev PD. Changes in insulin secretion and action in adults with familial risk for type 2 diabetes who curtail their sleep. Diabetes care. 2011;34:2259–64. [PubMed: 21836106]

[20]. Robertson MD, Russell-Jones D, Umpleby AM, Dijk DJ. Effects of three weeks of mild sleep restriction implemented in the home environment on multiple metabolic and endocrine markers in healthy young men. Metabolism: clinical and experimental. 2013;62:204–11. [PubMed: 22985906]

[21]. Donga E, van Dijk M, van Dijk JG, Biermasz NR, Lammers GJ, van Kralingen KW, et al. A single night of partial sleep deprivation induces insulin resistance in multiple metabolic pathways in healthy subjects. The Journal of clinical endocrinology and metabolism. 2010;95:2963–8. [PubMed: 20371664]

[22]. Matthews KA, Dahl RE, Owens JF, Lee L, Hall M. Sleep duration and insulin resistance in healthy black and white adolescents. Sleep. 2012;35:1353–8. [PubMed: 23024433]

[23]. De Bernardi Rodrigues AM, da Silva Cde C, Vasques AC, Camilo DF, Barreiro F, Cassani RS, et al. Association of Sleep Deprivation With Reduction in Insulin Sensitivity as Assessed by the Hyperglycemic Clamp Technique in Adolescents. JAMA pediatrics. 2016;170:487–94. [PubMed: 26999405]

[24]. Javaheri S, Storfer-Isser A, Rosen CL, Redline S. Association of short and long sleep durations with insulin sensitivity in adolescents. The Journal of pediatrics. 2011;158:617–23. [PubMed: 21146189]

[25]. Klingenberg L, Chaput JP, Holmback U, Visby T, Jennum P, Nikolic M, et al. Acute Sleep Restriction Reduces Insulin Sensitivity in Adolescent Boys. Sleep. 2013;36:1085–90. [PubMed: 23814346]

[26]. Baker FC, Driver HS. Circadian rhythms, sleep, and the menstrual cycle. Sleep medicine. 2007;8:613–22. [PubMed: 17383933]

[27]. Ancoli-Israel S, Martin JL, Blackwell T, Buenaver L, Liu L, Meltzer LJ, et al. The SBSM Guide to Actigraphy Monitoring: Clinical and Research Applications. Behavioral sleep medicine. 2015;13 Suppl 1:S4–s38. [PubMed: 26273913]

[28]. Crowley SJ, Van Reen E, LeBourgeois MK, Acebo C, Tarokh L, Seifer R, et al. A longitudinal assessment of sleep timing, circadian phase, and phase angle of entrainment across human adolescence. PloS one. 2014;9:e112199. [PubMed: 25380248]

[29]. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes care. 1999;22:1462–70. [PubMed: 10480510]

[30]. Gungor N, Saad R, Janosky J, Arslanian S. Validation of surrogate estimates of insulin sensitivity and insulin secretion in children and adolescents. The Journal of pediatrics. 2004;144:47–55. [PubMed: 14722518]

[31]. Allison DB, Paultre F, Maggio C, Mezzitis N, Pi-Sunyer FX. The use of areas under curves in diabetes research. Diabetes care. 1995;18:245–50. [PubMed: 7729306]

[32]. Bruni O, Ottaviano S, Guidetti V, Romoli M, Innocenzi M, Cortesi F, et al. The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. Journal of sleep research. 1996;5:251–61. [PubMed: 9065877]

[33]. Flint J, Kothare SV, Zihlif M, Suarez E, Adams R, Legido A, et al. Association between inadequate sleep and insulin resistance in obese children. The Journal of pediatrics. 2007;150:364–9. [PubMed: 17382111]

[34]. Koren D, Levitt Katz LE, Brar PC, Gallagher PR, Berkowitz RI, Brooks LJ. Sleep architecture and glucose and insulin homeostasis in obese adolescents. Diabetes care. 2011;34:2442–7. [PubMed: 21933909]

[35]. Sung V, Beebe DW, Vandyke R, Fenchel MC, Crimmins NA, Kirk S, et al. Does sleep duration predict metabolic risk in obese adolescents attending tertiary services? A cross-sectional study. Sleep. 2011;34:891–8. [PubMed: 21731139]

[36]. Dumin M, O'Sullivan K, Deplewski D, Van Cauter E, Koren D. 0911 Chronotype and Type 2 Diabetes Risk in Preadolescents. Sleep. 2017;40:A339.

[37]. Knutson KL, von Schantz M. Associations between chronotype, morbidity and mortality in the UK Biobank cohort. Chronobiology international. 2018:1–9.

[38]. Brum MC, Filho FF, Schnorr CC, Bottega GB, Rodrigues TC. Shift work and its association with metabolic disorders. Diabetology & metabolic syndrome. 2015;7:45. [PubMed: 25991926]

[39]. Eckel RH, Depner CM, Perreault L, Markwald RR, Smith MR, McHill AW, et al. Morning Circadian Misalignment during Short Sleep Duration Impacts Insulin Sensitivity. Current biology: CB. 2015.

[40]. Crowley SJ, Acebo C, Fallone G, Carskadon MA. Estimating dim light melatonin onset (DLMO) phase in adolescents using summer or school-year sleep/wake schedules. Sleep. 2006;29:1632–41. [PubMed: 17252895]

[41]. Crowley SJ, Carskadon MA. Modifications to weekend recovery sleep delay circadian phase in older adolescents. Chronobiology international. 2010;27:1469–92. [PubMed: 20795887]

[42]. Taylor A, Wright HR, Lack LC. Sleeping-in on the weekend delays circadian phase and increases sleepiness the following week. Sleep and Biological Rhythms. 2008;6:172–9.

[43]. Mizokami-Stout K, Cree-Green M, Nadeau KJ. Insulin resistance in type 2 diabetic youth. Current opinion in endocrinology, diabetes, and obesity. 2012;19:255–62.

[44]. School start times for adolescents. Pediatrics. 2014;134:642–9. [PubMed: 25156998]

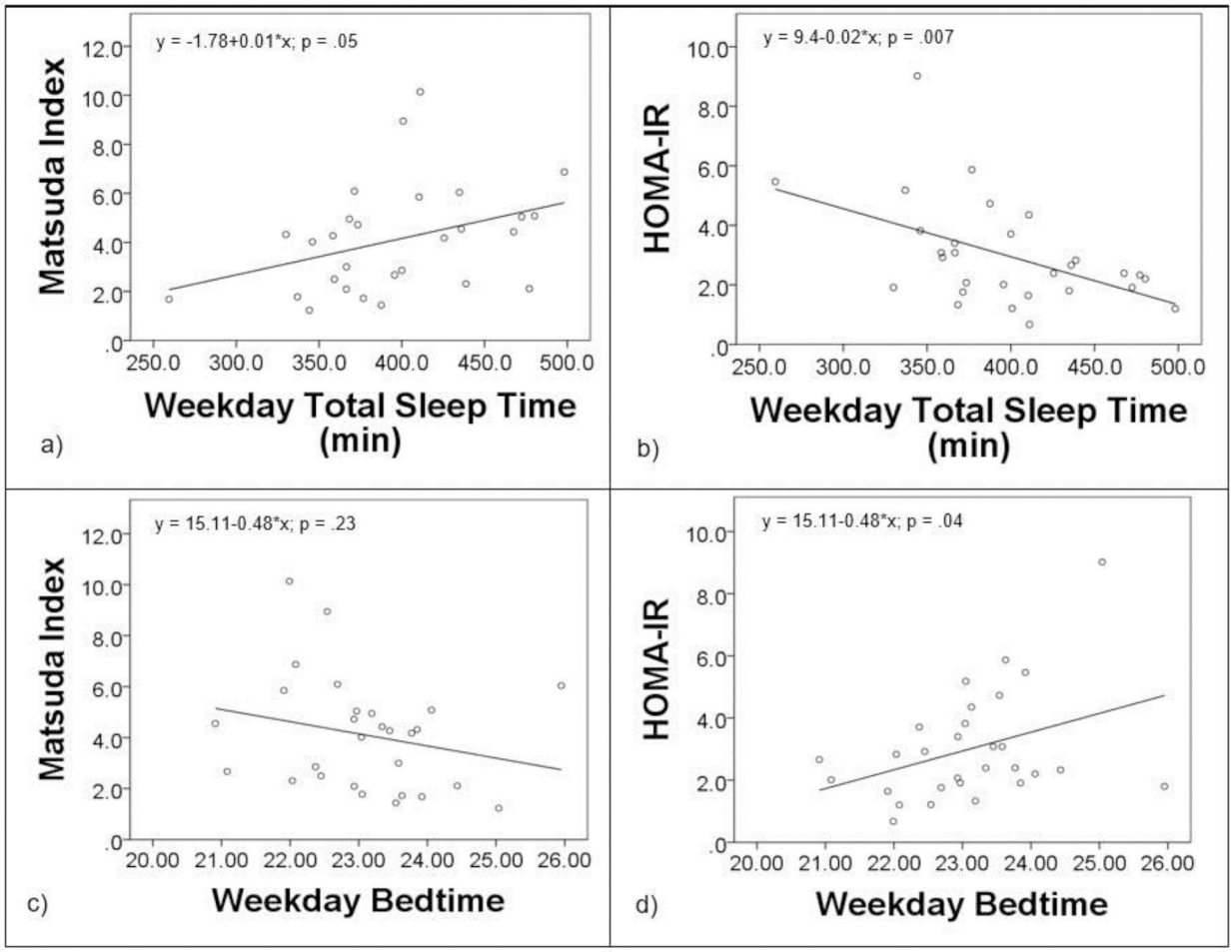

Figure 1.

Regression analyses between weekday total sleep time and a) Matsuda Index and b) HOMA-IR, and weekday bedtime and c) Matsuda Index and d) HOMA-IR. Greater weekday sleep duration and earlier bedtimes were significantly associated with better insulin sensitivity.

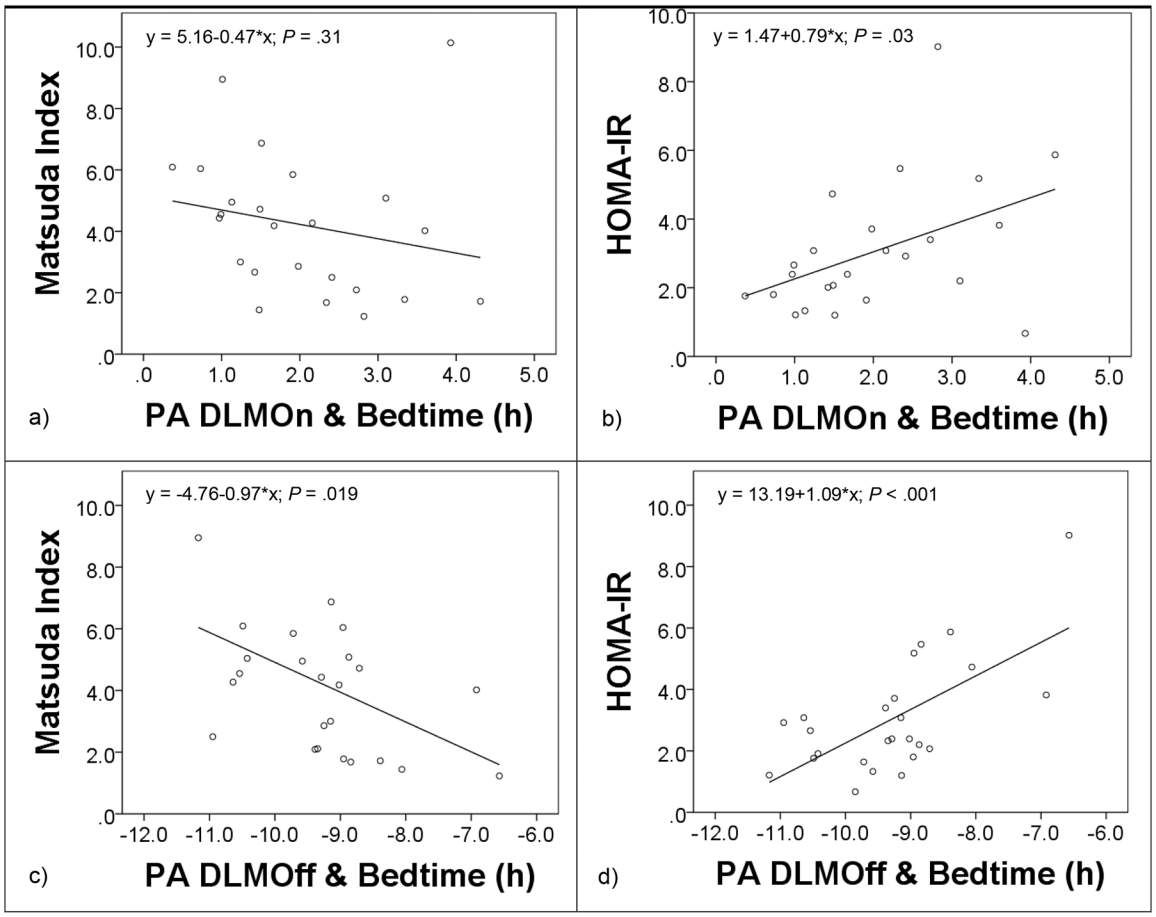

Figure 2.

Regression analyses between the phase angle (PA) for dim light melatonin onset (DLMOn) and bedtime and a) Matsuda Index and b) HOMA-IR, and PA for dim light melatonin offset (DLMOff) and bedtime and c) Matsuda Index and d) HOMA-IR. Shorter phase angles between weekday bedtime and DLMOn, indicating sleep onset at an earlier circadian time, were significantly associated with better S_i. Greater phase angles between weekday bedtime and DLMOff, reflecting longer sleep duration during the biological night, were significantly associated with better S_i.

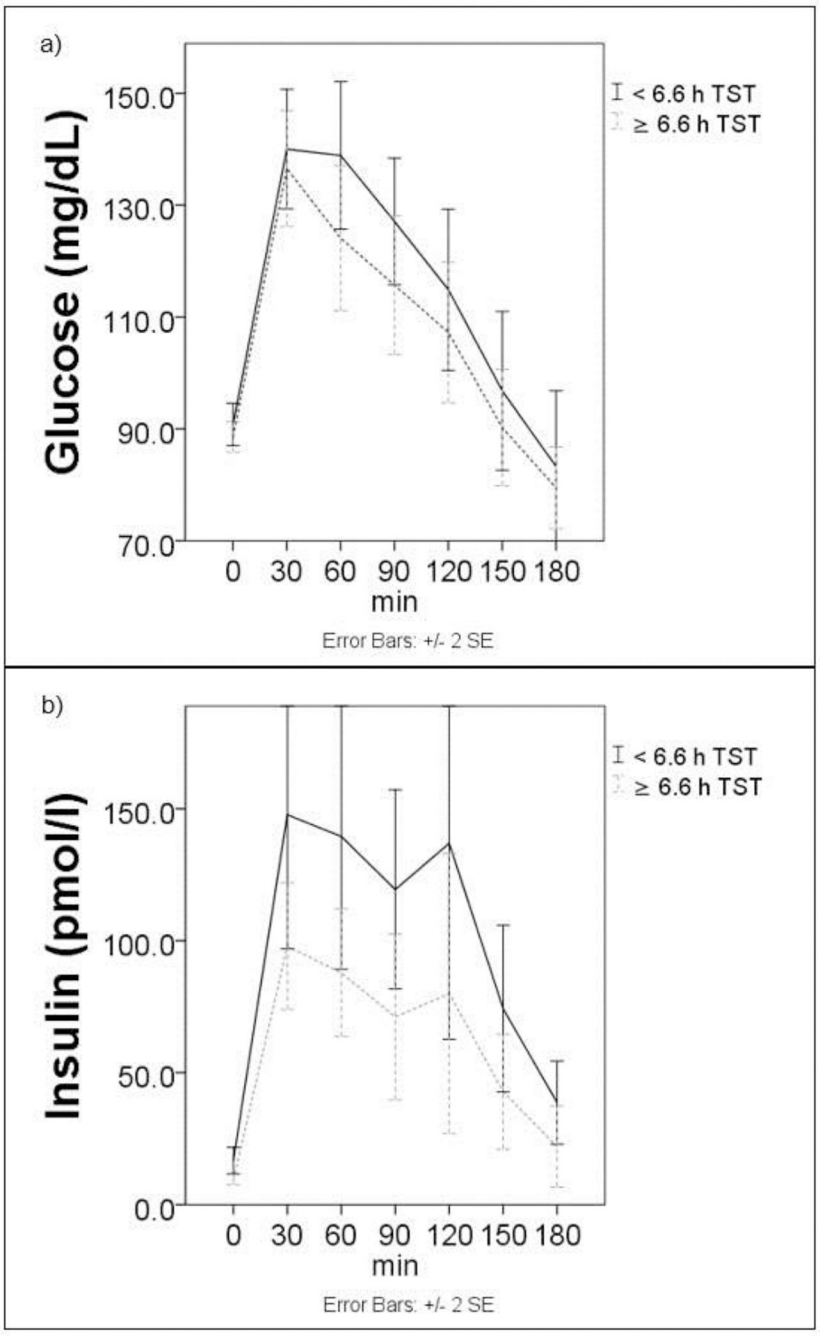

Figure 3.

Area under the curve for a) glucose and b) insulin concentrations. Participants with sleep duration less than the median of 6.6h per night had significantly greater area under the curve (AUC) for insulin ($p = 0.03$), but not glucose ($p = 0.2$), compared to those with ≥6.6h sleep per night.

Table 1.

Participant Characteristics, Mean (SD)

	N = 31
Age (years)	16.0 (1.4)
Female Sex	24 (77.4%)
BMI Percentile	96.9 (2.4)
Race N (%)	
Hispanic	18 (58.1)
African American	8 (25.8)
Caucasian	5 (16.1)
Tanner Stage N (%)	
4	9 (29)
5	22 (71)
Insulin Sensitivity	
HbA_1c	5.4 (0.3)
Matsuda Index	4.1 (2.2)
HOMA (mg/dl)	3.0 (1.8)

Table 2.

Actigraphy & Melatonin Variables, Mean (SD)

Actigraphy (N = 31)	*Weekday*	*Weekend*	*p*
Total Sleep Time (min)	396.4 (52.6)	450.3 (57.4)	**<.001**
Time in Bed (min)	471.17 (57.5)	545.46 (85.4)	**<.001**
Onset Latency (min)	17.3 (18.8)	15.9 (17.9)	.75
Sleep Efficiency (%)	84.5 (5.7)	83.1 (6.4)	.16
WASO (min)	49.7 (23.6)	70.1 (43.7)	**<.001**
Bedtime *M (min, max)*	23:03 (20:54, 01:57)	24:01 (20:31, 03:11)	**<.001**
Waketime *M (min, max)*	06:52 (05:31, 09:53)	09:06 (05:49, 12:14)	**<.001**
Midpoint Time *M (min, max)*	03:17 (01:37, 06:16)	05:04 (01:47, 08:53)	**<.001**
Melatonin (N = 27)	*Weekday*		
DLMOn (time)	21:00 (1.5 h)		
DLMOff (time)	08:24 (1.0 h)		
Bedtime PA DLMOn (h)	2.0 (1.0)		
Bedtime PA DLMOff (h)	−9.3 (1.1)		
Waketime PA DLMOn (h)	9.7 (1.1)		
Waketime PA DLMOff (h)	−1.6 (1.1)		
Duration melatonin secretion (h)	11.3 (1.2)		

P-value represents significant differences between weekday and weekend variables as assessed with paired samples t-tests

WASO, wake after sleep onset; DLMOn, dim light melatonin onset; DLMOff, dim light melatonin offset; PA, phase angle