Changes in Insulin Secretion and Action in Adults With Familial Risk for Type 2 Diabetes Who Curtail Their Sleep

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OBJECTIVE—Experimental sleep deprivation is accompanied by changes in glucose regulation. However, the effects of chronic sleep insufficiency on insulin secretion and action in populations at high risk for type 2 diabetes are not known. This study examined the relationship between objectively documented habitual sleep curtailment and measures of insulin sensitivity, insulin secretion, and oral glucose tolerance in free-living adults with parental history of type 2 diabetes.

RESEARCH DESIGN AND METHODS—A total of 47 healthy participants with parental history of type 2 diabetes (26 female/21 male, mean [SD] age 26 [4] years and BMI 23.8 [2.5] kg/m^2) completed 13 (SD = 2) days of sleep and physical activity monitoring by wrist actigraphy and waist accelerometry while following their usual lifestyle at home. Laboratory polysomnography was used to screen for sleep disorders. Indices of diabetes risk based on oral glucose tolerance tests were compared between participants with habitual short sleep and those with usual sleep duration >6 h/day.

RESULTS—Consistent with a behavioral pattern of habitual sleep curtailment, short sleepers obtained an average of 1.5 h less sleep per night and showed signs of increased sleep pressure. Participants who habitually curtailed their sleep had considerably higher indices of insulin resistance and increased insulin secretion but maintained normal glucose tolerance similar to that of subjects who slept more.

CONCLUSIONS—Young lean adults with parental history of type 2 diabetes who habitually curtail their sleep have increased insulin resistance and compensatory hyperinsulinemia—a pattern that has been associated with higher risk of developing diabetes in such susceptible individuals.

Driven by the demands and opportunities of modern life, many Americans today sleep <6 h/day (1). Self-reports of such short sleep have been associated with increased incidence of diabetes (2), which raises the possibility that chronic sleep insufficiency may affect factors involved in the pathogenesis of type 2 diabetes. Indeed, studies of healthy volunteers in the laboratory indicate that short-term sleep deprivation can modify systemic glucose tolerance, insulin secretion, or insulin action (3–8). However, the importance of these experimentally induced changes in insulin secretion or action for the association of self-reported short sleep with incident diabetes in free-living adults is not well defined. Furthermore, the impact of chronic sleep insufficiency on measures of glucose tolerance, pancreatic β-cell function, and insulin sensitivity in individuals with high preexisting risk of type 2 diabetes has not been studied. There is also concern that the relationship between self-reported short sleep and diabetes risk in epidemiological studies may harbor residual confounding by factors such as undiagnosed sleep problems (e.g., sleep apnea and insomnia), poor physical or emotional health, and systemic biases in the subjective recall of sleep and physical activity (1,9,10).

Healthy adults with parental history of type 2 diabetes have a high risk for developing the disease and exhibit changes in insulin secretion and action long before the onset of diabetes (11–16). Understanding whether objectively documented chronic sleep insufficiency can aggravate the preexisting defects in insulin sensitivity and β-cell function in such high-risk individuals may inform the development of improved behavioral strategies for metabolic risk reduction. The goal of this exploratory study was to collect objective measures of habitual sleep duration and free-living physical activity and test the hypothesis that healthy adults with parental history of type 2 diabetes who curtail their sleep will show signs of increased insulin resistance. Secondary end points included measures of insulin secretion and oral glucose tolerance.

RESEARCH DESIGN AND METHODS

Healthy men and women aged 21–40 years with a BMI between 19 and 27 kg/m^2 who had at least one parent with type 2 diabetes were recruited through local advertisements. Fasting body weight and height were measured in the morning using a calibrated scale (Scale-Tronix Inc., Wheaton, IL) and stationary Harpenden stadiometer (Holtain, Crymych, Wales). We excluded subjects who had any acute or chronic medical condition; self-reported sleep problems (Pittsburgh Sleep Quality Index global score >6), night work, or habitual daytime naps; recent (<4 weeks) travel across time zones; history of irregular menstrual periods, pregnancy, or childbirth during the past year; depressed mood (Center for Epidemiologic Studies of Depression score >15 confirmed by clinical interview); current tobacco use or excessive alcohol intake (>14 drinks/week for men; >7 for women); use of prescription, over-the-counter, or illegal drugs and supplements that can affect sleep or metabolism; and abnormal findings on physical exam or laboratory testing, including complete blood counts, comprehensive metabolic panel, thyroid function tests, 12-lead

electrocardiogram, and a 75-g oral glucose challenge. The study protocol was registered and approved by the institutional review board of the University of Chicago. Research volunteers gave written informed consent and were paid for their participation.

Habitual sleep and physical activity monitoring

Participants were asked to complete 14 days of sleep monitoring while following their usual lifestyle at home. A small accelerometer equipped with an event marker (Actiwatch-64, Mini-Mitter-Respironics, Bend, OR) was attached with a wrist band to the nondominant arm and actigraphy data were collected continuously in 1-min epochs to measure usual sleep duration under free-living conditions (1). Since reduction in physical activity related to sleep loss may contribute to the association of short sleep with metabolic morbidity, we also measured the amount and intensity of body movement of each participant using a small accelerometer (Actical, Mini-Mitter-Respironics) attached with an elastic waistband over the iliac crest. Detailed physical activity data from a subset of the participants in this study have been reported elsewhere (17). To be included in the analysis, participants were required to wear the Actiwatch for at least seven full nights and the Actical for at least six full days. A total of 61 subjects were enrolled; 8 discontinued their participation before completing the study (because of new job, family illness, or moving), 4 had <6 days of recording, and 2 had problems with the intravenous catheter during the glucose tolerance test and were excluded. The remaining 47 study participants completed an average of 13 (SD = 2) days of home monitoring.

Nighttime sleep was scored automatically with Actiware Sleep version 3.4, provided with the Actiwatch, using a medium sensitivity setting of 40. Habitual sleep duration was calculated as the average number of minutes scored as sleep across all recorded nights. Actical data were analyzed using version 2.12 of the software provided with the device. Results were averaged across all recorded days to obtain individual measures of the average daily time spent in physical activity of moderate-and-vigorous intensity.

Polysomnography

After their home monitoring period, participants were scheduled to complete one night of laboratory polysomnography (Neurofax-1100 EEG Acquisition System,

Nihon-Kohden, Foothill Ranch, CA) including electroencephalography, electrooculography, electromyography, airflow, thoracic and abdominal respiratory effort, electrocardiography and pulse oximetry to exclude the presence of primary sleep pathology, sleep movement disorder, or sleep disordered breathing (respiratory disturbance index >10). Overnight recordings were obtained in 41 subjects (87%) who kept their study appointments (Table 1). Sleep was scheduled between 2300–2400 h and 0730–0830 h with a fixed time in bed of 8.5 h. Records were scored in 30-s epochs of wake; movement; stage 1, 2, 3, and 4 sleep; and rapid eye movement (REM) sleep according to standard criteria. Respiratory events, periodic leg movements, and arousals were scored using current clinical guidelines. Total sleep time was calculated as the sum of all epochs scored as sleep. Sleep efficiency was calculated as the percent of scheduled time in bed that was scored as sleep. Sleep onset latency was defined as the time between lights-off and the first epoch of stage 1 sleep.

Measures of glucose tolerance, insulin secretion, and insulin action

A distal forearm intravenous catheter was placed upon the arrival of each participant in the morning after an overnight fast. An oral glucose tolerance test (OGTT) was started half an hour later. Two baseline blood samples were collected (−15 and 0 min) for measurement of glucose and insulin, and 75 g dextrose dissolved in 296 cc of orange-flavored water (NERL Diagnostics LLC, East Providence, RI) was ingested in <5 min. Additional blood samples were collected at 30, 60, 90, 120, 150, and 180 min. Plasma glucose was measured with STAT-2300 analyzer (Yellow Spring Instruments, Yellow Springs, OH). Serum insulin was measured using human chemiluminescent immunoassay (Immulite-2000, Diagnostic Products, Los Angeles, CA). Fasting glucose and insulin concentrations were calculated as the average of the −15 and 0-min readings.

Measures of glucose tolerance included fasting and 2-h plasma glucose concentrations, the area under the 3-h OGTT curve for glucose (calculated using the trapezoidal method), and hemoglobin A_{1c}. The measures of insulin action were 1) the homeostasis model assessment index of insulin resistance (HOMA-IR) calculated using fasting glucose and insulin concentrations (HOMA2 Calculator v.2.2 at http://www.dtu.ox.ac.uk/homa; Diabetes Trials Unit, University of Oxford,

Oxford, U.K.) and 2) the insulin sensitivity index (ISI) based on glucose (mg/dL) and insulin concentrations (mU/L) during the OGTT as described by Matsuda et al. (18). The corrected insulin response to glucose, CIR = (100 × insulin [pmol/L] at 30 min)/(glucose [mmol/L] at 30 min × (glucose [mmol/L] at 30 min − 3.89 mmol/L)), and the area under the 3-h OGTT curve for insulin were used as measures of insulin secretion (19). Corresponding CIR and ISI values were multiplied to calculate a disposition index (DI = CIR × ISI) to assess the compensation of insulin secretion for the degree of individual insulin resistance (20).

Data analysis and statistics

Family risk for diabetes was classified as 1) increased (one parent with type 2 diabetes or one parent and one 2nd-degree relative with type 2 diabetes) or 2) high (at least two 1st-degree relatives—two parents or parent and sibling—or one parent and at least two 2nd-degree relatives with type 2 diabetes from the same lineage) (21). African, Hispanic, and Asian American participants were considered to have higher race/ethnicity-related risk of type 2 diabetes compared with Caucasians. Self-reported sleep duration was measured with the question, "How many hours of actual sleep did you get at night during the past month?" The Pittsburgh Sleep Quality Index was used to measure subjective sleep quality and the Epworth Sleepiness Scale was used to assess daytime sleepiness. Higher scores on both of these scales reflect worse subjective ratings.

Two separate approaches were used to examine the association of objectively measured habitual sleep duration with measures of insulin resistance, insulin secretion, and oral glucose tolerance. To accommodate for the analysis of multiple end points, each approach followed a gatekeeping strategy in which the primary outcome measure was tested first, followed by additional analyses with adjustment for multiple comparisons only if the initial gatekeeping test was significant (22).

First, we generated a set of multiple linear regression models to examine the role of objectively measured sleep duration as a predictor of insulin sensitivity (ISI as primary outcome measure) and six ancillary measures of insulin resistance, insulin secretion, and oral glucose tolerance in the study sample while controlling for the independent contributions of participant age; BMI; sex; African American, Asian, and Hispanic race/ethnicity (three

Table 1—*Descriptive characteristics of the participants and their sleep*

	All	Short sleep	Sleep >6 h/day	P value
Participants (*n*)	47	15	15	
Age (years)	26 ± 4	28 ± 5	26 ± 3	0.137
BMI (kg/m^2)	23.8 ± 2.5	24.3 ± 1.9	23.9 ± 2.8	0.628
Sex distribution (female/male)	26/21	9/6	9/6	1.000
African American/Asian/Hispanic (*n*)	12/7/4	5/3/2	5/4/1	0.679
Family diabetes risk (increased/high)	34/13	10/5	11/4	0.690
Women in luteal phase of menstrual cycle (*n*)	10	3	5	0.403
Level of education (years)	17 ± 2	16 ± 2	17 ± 2	0.478
Caffeine intake (mg/day)	118 ± 159	171 ± 194	140 ± 184	0.812#
Alcohol consumption (g/week)	22 ± 31	16 ± 16	26 ± 46	0.918#
Self-reported sleep				
Duration (min/day)	456 ± 58	422 ± 58	468 ± 47	0.024
Epworth Sleepiness Scale score	6.0 ± 3.5	7.4 ± 3.6	4.6 ± 2.6	0.022
Pittsburgh Sleep Quality Index score	2.6 ± 1.5	2.6 ± 1.8	2.3 ± 1.1	0.506
Measured sleep and activity				
Length of monitoring (days)	13 ± 2	14 ± 1	14 ± 2	
Average sleep duration (min/day)	373 ± 55	316 ± 27	405 ± 35	<0.001
Moderate-and-vigorous activity (min/day)	139 ± 54	122 ± 35	164 ± 68	0.040
Laboratory polysomnography				
Participants (*n*)	41	12	13	
Length of recording (h:min)	8:29 ± 0:25	8:18 ± 0:35	8:28 ± 0:20	0.431
Sleep onset latency (min)	25 ± 30	24 ± 29	18 ± 17	0.546#
REM sleep latency (min)	105 ± 52	81 ± 42	119 ± 63	0.095
Arousal index (events/h)	14 ± 7	12 ± 4	15 ± 9	0.401
Sleep efficiency (%)	88 ± 8	89 ± 9	89 ± 6	0.814
Wake (min)	63 ± 42	53 ± 47	56 ± 29	0.826
Stage 1 sleep (min)	31 ± 15	33 ± 16	32 ± 14	0.891
Stage 2 sleep (min)	263 ± 37	254 ± 36	269 ± 32	0.265
Slow-wave sleep (min)	52 ± 29	59 ± 29	49 ± 29	0.397
REM sleep (min)	97 ± 31	97 ± 32	93 ± 29	0.779
Total sleep (min)	443 ± 49	443 ± 55	444 ± 42	0.944
RDI (events/h)	2 ± 3	3 ± 4	2 ± 3	0.951

Data are mean ± SD. *P* values reflect comparisons between participants with habitual short sleep and matched subjects with sleep duration >6 h/day using Pearson χ^2 test for categorical and Student independent-samples test for continuous variables. RDI, respiratory disturbance index. #Square root–transformed data used for comparison.

binary variables); and familial diabetes risk (increased or high). The level of statistical significance was set at $P < 0.05$ for our gatekeeping analysis of ISI and $P \leq 0.008$ for each secondary end point (HOMA-IR, CIR, fasting and 2-h blood glucose, and the areas under the 3-h OGTT curve for glucose and insulin). Since short sleep duration was accompanied by reduced physical activity (Table 1), we reexamined these associations when control for time spent in physical activity of moderate-and-vigorous intensity was added to the initial regression model (Table 2).

Second, since sleeping <6 h/day has been associated with increased risk of diabetes (2), study participants were classified according to their objectively measured sleep time at home as either short sleepers with average sleep time <6 h/day (*n* = 19) or reference sleepers with average sleep ≥6 h/day (*n* = 28). To compare the patterns of

glucose regulation between short and reference sleepers, we selected 15 participants whose sleep duration was in the lowest tertile of the study sample and matched them as closely as possible by age, BMI, sex, race/ethnicity, and family risk for diabetes to a group of 15 participants with habitual sleep duration >6 h/day (Table 1). The primary outcome variable (ISI) and four secondary measures selected based on the outcomes of the previous regression analysis (HOMA-IR, CIR, area under the 3-h OGTT insulin curve, and fasting insulin) were compared between the two groups using ANCOVA, controlling for time spent in physical activity of moderate-and-vigorous intensity (Table 3). Although the difference was not statistically significant, short sleepers were slightly older (26 ± 3 vs. 28 ± 5 years; *P* = 0.137), and we repeated the ANCOVA after entering age as an additional covariate to minimize its influence

(Table 3). The level of statistical significance was set at $P < 0.05$ for our gate-keeping analysis of ISI and $P \leq 0.012$ for each secondary end point. HOMA-IR and fasting insulin were not normally distributed (Kolmogorov-Smirnov test $P < 0.05$) and were square root transformed for these comparisons. Statistical analyses were conducted with SPSS v.18.0 (SPSS Inc., Chicago, IL). Results are reported as mean ± SD.

RESULTS—Multiple linear regression analysis showed a significant association between reduced sleep duration and increased insulin resistance (lower ISI) in the entire study sample independent of age, BMI, sex, race/ethnicity, familial diabetes risk, and daily time spent in physical activity of moderate-and-vigorous intensity (Table 2). Regression analyses of secondary end points confirmed this finding using

Table 2—*Association of objectively measured sleep duration with insulin sensitivity and secondary measures of insulin secretion and glucose tolerance*

	Model 1	Model 2
ISI		
B	**2.3**	**2.5**
95% CI	(0.6–4.0)	(0.8–4.2)
P	0.009	0.006
HOMA-IR		
B	**−0.24**	**−0.27**
95% CI	(−0.08 to −0.40)	(−0.11 to −0.43)
P	0.004	0.001
3-h AUC insulin (pmol $\cdot$ L^{-1} $\cdot$ min^{-1})		
B	**−13,390**	**−13,793**
95% CI	(−5,054 to −21,726)	(−5,437 to −22,150)
P	0.003	0.002
CIR		
B	**−877**	**−868**
95% CI	(−409 to −1,345)	(−387 to −1,350)
P	0.001	0.001
Fasting blood glucose (mg/dL)		
B	−0.04	0.1
95% CI	(−2 to 2)	(−2 to 2)
P	0.966	0.898
3-h AUC glucose (mg $\cdot$ dL^{-1} $\cdot$ min^{-1})		
B	−227	−225
95% CI	(−1,084 to 629)	(−1,106 to 657)
P	0.594	0.609
Hemoglobin A$_{1c}$ (%)		
B	−0.04	−0.03
95% CI	(−0.1 to 0.04)	(−0.1 to 0.04)
P	0.311	0.442

Multiple linear regression analysis was used to assess the role of objectively measured habitual sleep duration as an independent predictor of insulin sensitivity (ISI as a primary outcome variable) and six secondary measures of insulin resistance, insulin secretion, and oral glucose tolerance in all participants ($N = 47$). Model 1 included control for age; BMI; sex; familial diabetes risk (elevated or high); and African American, Asian, and Hispanic race/ethnicity (binary variables) as other well-established independent predictors. Model 2 also controlled for the average daily time spent in physical activity of moderate-and-vigorous intensity in addition to the predictors included in Model 1. B, regression coefficient reflecting the change in the corresponding dependent variable for each 1-h increase in habitual sleep duration (boldface numbers show significant associations); AUC, area under the curve during the OGTT.

HOMA-IR as a measure of insulin resistance and showed that participants with shorter sleep duration had higher indices of insulin secretion (CIR and area under the 3-h OGTT curve for insulin) (Table 2). There was no significant association between objectively measured sleep duration and markers of glucose tolerance (Table 2). The addition of control for alcohol and caffeine consumption in these models produced similar results (data not shown).

During an average night at home, the 15 participants with measured sleep duration in the lowest tertile of the study sample obtained 1 h 29 min less sleep ($P < 0.001$) compared with the group of 15 reference sleepers with similar age, BMI, sex, race/ethnicity, and family risk for diabetes (Table 1). Self-reported sleep exceeded objectively measured sleep

duration in both groups (Table 1), but short sleepers overestimated their usual sleep duration considerably more than the participants in the reference group (average overreporting: 106 ± 58 vs. 63 ± 42 min/day; $P = 0.026$). Both groups had good subjective sleep quality (Table 1); however, short sleepers reported significantly more daytime sleepiness ($P = 0.022$). When time in bed was fixed to 8.5 h in the laboratory, the measured quantity and quality of sleep of the short sleepers was comparable to that of the reference sleep group (Table 1). Consistent with the presence of increased sleep pressure, short sleepers tended to have faster onset of REM sleep ($P = 0.095$) (Table 1).

Compared with the subjects in the reference group, short sleepers had significantly lower ISI and higher HOMA-IR

(Table 3). The 32% lower index of insulin sensitivity in the short-sleep group was accompanied by higher fasting insulin and CIR values and a larger area under the 3-h OGTT insulin curve (Table 3). Participants in the short- and reference sleep groups had comparable DI (13,784 ± 8,565 and 14,046 ± 9,312), fasting (87 ± 7 and 84 ± 6 mg/dL) and 2-h blood glucose (105 ± 21 and 101 ± 15 mg/dL), and area under the 3-h OGTT glucose curve (19,257 ± 2,059 and 17,800 ± 2,206 mg $\cdot$ dL^{-1} $\cdot$ min^{-1}).

CONCLUSIONS—This study examined the relationship between objectively documented reduced sleep duration and OGTT-based measures of insulin sensitivity, insulin secretion, and glucose tolerance in healthy free-living adults with parental history of type 2 diabetes. Consistent with previous population-based data (1), 40% of the participants in our convenience sample had habitual sleep duration <6 h/day. Compared with their counterparts in the reference group, participants in the short-sleep group obtained an average of 1.5 h less sleep per night. However, when assessed formally by polysomnography, short sleepers did not have any sleep problems or biologically lower need to sleep (Table 1). Instead, they reported significantly more daytime sleepiness consistent with the presence of a behavioral pattern of habitual sleep curtailment and chronic sleep debt. Study participants who habitually curtailed their sleep in this fashion were considerably more insulin resistant (Table 2). The increased insulin resistance of the short sleepers was associated with a compensatory rise in insulin secretion (Table 3), which allowed them to maintain normal glucose tolerance similar to that of the participants in the reference sleep group.

Adults with parental history of type 2 diabetes have decreased insulin-mediated glucose disposal and nonoxidative glucose metabolism compared with individuals without family history of diabetes (11,13,14). Our data indicate that this insulin resistance may be considerably higher among those members of this group who habitually curtail their sleep. Several laboratory experiments have documented that short-term sleep deprivation can result in reduced systemic insulin sensitivity, and some have speculated that this may be related to changes in adrenocortical or autonomic nervous system activity (3,5–8). Whether similar mechanisms may contribute to the increased insulin resistance in free-living

Table 3—*Measures of insulin sensitivity and insulin secretion in participants with habitual short sleep and matched control subjects who sleep >6 h/day*

	Sleep >6 h/d	Short sleep	P value*	P value†
Primary outcome measure				
ISI	11.4 ± 5.6	7.7 ± 4.3	0.033	0.013
Secondary end points				
HOMA-IR	0.46 ± 0.28	0.81 ± 0.70	0.009#	0.001#
Fasting insulin (pmol/L)	25 ± 15	44 ± 38	0.010#	0.001#
3-h AUC insulin				
(pmol · L^{-1} · min^{-1})	36,992 ± 13,306	52,895 ± 30,208	0.050	0.008
CIR	1,490 ± 1,124	2,570 ± 2,370	0.116	0.007

Data are mean ± SD (n = 15 in each group). AUC, area under the curve during the OGTT. *P values based on ANCOVA with sleep group (short vs. control) as a between-subject factor controlling for daily time spent in physical activity of moderate-and-vigorous intensity, which was included as a covariate. †P values based on ANCOVA as in * with additional control for participant age, which was included as a covariate. #Square root–transformed data used for comparison.

adults who habitually curtail their sleep has not been studied. Other determinants of systemic insulin resistance include obesity, advancing age, and familial and ethnic risk factors. However, short sleep duration was found to predict the presence of increased insulin resistance when the contribution of these factors was controlled for in our multiple regression analysis (Table 2).

It is notable that short sleepers had lower levels of physical activity of moderate-and-vigorous intensity (Table 1). Nevertheless, inclusion of the average daily time spent in moderate-and-vigorous activity as an independent variable in our multiple regression analysis did not attenuate the association between objectively measured short sleep duration and increased insulin resistance (Table 2). The 32% difference in insulin sensitivity between otherwise comparable groups of short and reference sleepers was also statistically significant when time spent in moderate-and-vigorous activity was entered in that analysis as a covariate (Table 3). Results were similar when we used daily counts of total body movement instead of the average time spent in moderate-and-vigorous physical activity (data not shown). Despite this, our findings remain compatible with the possibility that longer-term effects of physical activity on predictors of insulin resistance, such as aerobic fitness, metabolic flexibility, and accumulation of fat in visceral and ectopic organ sites, may explain some of the association between habitual sleep duration and ISI. Reduced physical fitness and total aerobic capacity, lower resting metabolic rate, increased abdominal adiposity, and defects in lipid metabolism have been described in healthy normoglycemic

offspring of type 2 diabetic parents (13,15,16,23). Since chronic sleep insufficiency alone, or in association with lower physical activity, may have an adverse effect on these variables (8,24,25), additional studies are needed to define the metabolic risk profile of habitual sleep curtailment in this high-risk population. Irrespective of the underlying mechanisms, the finding that healthy lean adults with parental history of type 2 diabetes who habitually sleep <6 h/day are considerably more insulin resistant compared with those who obtain more sleep may have important health implications. Since insulin resistance is a strong predictor of diabetes incidence in the offspring of type 2 diabetic parents (11), a behavioral pattern of habitual sleep curtailment in this group may be associated with a higher risk of developing the disease relative to the risk conferred by family history alone (2).

The maintenance of normal glucose homeostasis involves reciprocal changes in insulin secretion and sensitivity (20). The young and lean short sleepers in our study were able to secrete more insulin to compensate for their higher insulin resistance (Tables 2 and 3). Some studies of experimental sleep deprivation in healthy volunteers have observed similar changes in insulin secretion and sensitivity (3,8), whereas others found reduced glucose tolerance and either unchanged or decreased insulin secretion (4–6). Individuals with parental history of type 2 diabetes can exhibit deficits in insulin secretion long before the development of overt diabetes, and progressive loss of β-cell function is another key factor for the development of type 2 diabetes in this susceptible population (12,15,16). Our findings now raise the question

whether the demand for increased insulin secretion related to higher insulin resistance in at-risk adults who habitually curtail their sleep may result in earlier β-cell failure as they grow older, gain excess weight, and continue to maintain a more sedentary lifestyle.

Our study has several strengths and limitations. We collected proof-of-concept data from a carefully screened sample of healthy individuals at risk for type 2 diabetes, while avoiding the confounding effects of obesity and poor general or emotional health. The use of laboratory polysomnography and objective monitoring of habitual sleep and free-living physical activity also allowed us to exclude the presence of sleep pathology and avoid assessments based on unreliable self-reports of these behaviors (see RESULTS for an example of systemic bias in self-reported sleep). Finally, it was important to study a population with high risk for type 2 diabetes, which may inform future behavioral research on sleep and metabolic risk reduction. Despite its strengths, this was an exploratory study that included a relatively small number of subjects and used indirect OGTT-based techniques to assess insulin secretion and sensitivity. Although our free-living sleep data were similar to those of other population-based reports (1), study participants were not randomly selected and results may not be entirely representative of the relationship between sleep and insulin sensitivity in this high-risk group.

In conclusion, a large number of healthy young adults with familial risk for type 2 diabetes habitually curtail their sleep. Compared with a similar group of participants with parental history of type 2 diabetes and habitual sleep ≥6 h/day, those who slept less were considerably more insulin resistant and had increased insulin secretion—a pattern that has been associated with a higher risk of developing diabetes in this population (11). Future studies are needed to elucidate the link between habitual sleep curtailment as a behavioral risk factor for insulin resistance and increased metabolic morbidity in individuals with familial predisposition for type 2 diabetes.

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