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Brief Reports

Habitual shortened sleep and insulin resistance: An independent relationship in obese individuals

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ABSTRACT

Objective. Short sleep duration has been reported to be associated with obesity, type 2 diabetes, and pre-diabetes. Since excess weight, glucose abnormalities, and insulin resistance tend to cluster, the individual role insulin resistance may have in habitual shortened sleep is unclear. The study purpose was to assess whether habitual sleep curtailment is independently related to insulin resistance in obese individuals.

Materials/Methods. Non-diabetic, overweight/obese individuals from the community were stratified as insulin-resistant (n = 35) or insulin-sensitive (n = 21) based on steady-state plasma glucose concentrations (SSPG) during the insulin suppression test. Seventy-five gram oral glucose tolerance tests were performed. Participants were asked, "On average, how many hours of sleep do you get per night?" Shortened sleep duration was defined as less than 7 h of sleep per night.

Results. SSPG concentrations differed 2.5-fold ($P < 0.001$) between insulin-resistant and insulin-sensitive individuals. Impaired fasting glucose and glucose intolerance were prevalent in both groups (>40%); however, body mass index, waist circumference, mean fasting or 2-h post-glucola glucose concentrations were not significantly different. Insulin-resistant individuals reported (mean ± SD) fewer hours of sleep than did insulin-sensitive individuals (6.53 ± 1.1 vs 7.24 ± 0.9 h, $P < 0.05$). Shortened sleep duration was more prevalent among insulin-resistant as compared with insulin-sensitive individuals (60% vs 24%, $P < 0.05$).

Conclusions. Non-diabetic, insulin-resistant individuals averaged fewer hours of sleep and were more likely to report shortened sleep duration as compared with similarly obese insulin-sensitive individuals. There appears to be an independent association between habitual shortened sleep and insulin resistance among obese, dysglycemic adults without diabetes.

1. Introduction

Type 2 diabetes (T2DM) is estimated to affect more than 20 million Americans, and is associated with considerable morbidity and mortality. Given projections that prevalence of T2DM may double by 2050 [1], present efforts at risk modification are paramount. The potential association of short sleep with T2DM has come to recent attention [2]. The

Abbreviations: HOMA-IR, Homeostasis Model Assessment of Insulin Resistance; OSA, obstructive sleep apnea; SSPG, steady-state plasma glucose; T2DM, type 2 diabetes.

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trend over the past decades has seen Americans receiving fewer hours of sleep than they did previously [3,4]. Observational studies have suggested that short sleep duration may be linked to obesity [5], prediabetes [2,6], and insulin resistance [7,8]. Given that excess weight, glucose abnormalities, and insulin resistance tend to cluster together, it is not clear whether habitual shortened sleep is associated with insulin resistance, independent of adiposity or dysglycemia. To test this hypothesis, we compared self-reported sleep duration in individuals within a similar BMI range, divided into insulin-resistant and insulin-sensitive subgroups by a direct measurement of insulin-mediated glucose uptake. Oral glucose tolerance tests were also performed to evaluate further glucose metabolism.

2. Methods

Volunteers (n = 104) from the San Francisco Bay area were recruited consecutively in response to advertisements for our research studies on insulin resistance. Study protocols were approved by the Stanford Administrative Panels for the Protection of Human Subjects. All participants gave informed consent. Inclusion criteria included apparently healthy individuals without known diabetes, liver, kidney, or heart disease. They were selected to be moderately overweight to obese (body mass index [BMI] 27.0–34.9 kg/m^2). Individuals with known obstructive sleep apnea (OSA) or depression (self-reported depression and/or taking medications for treatment of depression) were excluded, leaving an experimental cohort of 78 individuals. Waist circumference was measured midway between the iliac crest and rib cage at end-expiration. Fasting lipid/lipoprotein concentrations were measured by conventional methods. A 75-g glucola drink was administered after a 12-h overnight fast. Glucose measurements were obtained before and 2 h after glucola ingestion. Impaired fasting glucose and impaired glucose tolerance were defined as plasma glucose ≥ 100 mg/dL and ≥ 140 mg/dL, respectively.

Insulin-mediated glucose uptake was quantified by the modified [9] insulin suppression test [10], which is highly correlated ($r > 0.9$) with the euglycemic clamp [10]. After an overnight fast, individuals were infused with octreotide (0.27 μg/m^2/min), insulin (32 mU/m^2/min), and glucose (267 mg/m^2/min) over 180 min. Plasma glucose and insulin concentrations were measured every 10 min during the final 30 min and averaged to obtain steady-state plasma glucose (SSPG) and insulin concentrations. Because steady-state plasma insulin concentrations are similar for all individuals, SSPG provides a direct measure of the ability of insulin to mediate disposal of the infused glucose load. Thus, the higher the SSPG, the more insulin-resistant the individual. Cut-points to identify insulin-resistant and insulin-sensitive individuals were defined as SSPG ≥ 180 mg/dL and ≤ 120 mg/dL, respectively, based on prospective studies demonstrating that clinical syndromes associated with insulin resistance occur in those classified as insulin-resistant and not in the insulin-sensitive subgroup [11], as well as a prior study of the distribution of SSPG concentrations in a reference population [12]. Applying these cut-points to the 78 participants evaluated, 56 were classified as being either insulin-resistant (n = 35) or insulin-sensitive (n = 21). The remaining participants were determined to be intermediate, and not further studied.

Participants were asked by written questionnaire, "On average, how many hours of sleep do you get per night?" Responses were allowed to be reported in half-hour increments. Shortened sleep duration was defined as fewer than 7 h of sleep per night.

Data analyses were performed using SPSS 20.0 (Chicago, IL). Between-group comparisons were made using *t*-tests for continuous variables. Categorical variables were compared using chi-square or Fisher's exact tests. Triglyceride, HDL-cholesterol, and LDL-cholesterol concentrations were log transformed to improve normality. Linear and logistic regression analyses were conducted to adjust for BMI. Statistical significance was defined as $P < 0.05$.

3. Results

Characteristics of the 56 participants are shown in Table 1. By selection, insulin-mediated glucose uptake differed substantially between the insulin-resistant and insulin-sensitive subgroups (2.5-fold, $P < 0.001$). Insulin-resistant individuals had somewhat higher values for BMI ($P = 0.07$). Dysglycemia was prevalent in both groups (>40% had impaired fasting glucose and/or glucose tolerance). However the 2 groups did

Table 1 – Characteristics of insulin-sensitive and insulin-resistant individuals.

Variable	Insulin-sensitive Individuals	Insulin-resistant Individuals	P
n	21	35	
Steady-state plasma glucose (mg/dL)	91 ± 21	220 ± 26	<0.001
Number of Men/Women	8/13	15/20	0.79
Race (White/Asian/Hispanic or Latino/Black or African–American/Mixed)	18W/2A/1H	18W/9A/5H/2B/1M	0.13
Age (years)	55 ± 9	56 ± 9	0.76
BMI (kg/m^2)	30.5 ± 2.5	31.6 ± 2.1	0.07
Waist circumference (cm)	102 ± 10	106 ± 8	0.12
Fasting glucose (mg/dL)	100 ± 7	102 ± 8	0.34
% Impaired fasting glucose	47.6	54.3	0.78
Glucose 2-h post 75 g glucola (mg/dL)	126 ± 33	142 ± 34	0.10
% Impaired glucose tolerance	42.9	48.6	0.79
Systolic blood pressure (mm Hg)	122 ± 12	129 ± 15	0.06
Diastolic blood pressure (mm Hg)	73 ± 8	77 ± 9	0.16
Total cholesterol (mg/dL)	187 ± 38	194 ± 37	0.50
LDL-cholesterol (mg/dL)	115 ± 33	113 ± 31	0.84
HDL-cholesterol (mg/dL)	56 ± 11	49 ± 14	0.04
Triglycerides (mg/dL)	83 ± 41	158 ± 74	<0.001

Data are means ± SD unless otherwise specified.
BMI, Body Mass Index; HDL, High-Density Lipoprotein; LDL, Low-Density Lipoprotein.