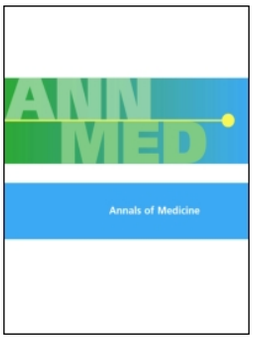

Annals of Medicine

ISSN: 0785-3890 (Print) 1365-2060 (Online) Journal homepage: informahealthcare.com/journals/iann20

Sleep duration and insulin resistance in individuals without type 2 diabetes: The PPP-Botnia Study

Antti-Jussi Pyykkönen, Bo Isomaa, Anu-Katriina Pesonen, Johan G. Eriksson, Leif Groop, Tiinamaija Tuomi & Katri Räikkönen

To cite this article: Antti-Jussi Pyykkönen, Bo Isomaa, Anu-Katriina Pesonen, Johan G. Eriksson, Leif Groop, Tiinamaija Tuomi & Katri Räikkönen (2014) Sleep duration and insulin resistance in individuals without type 2 diabetes: The PPP-Botnia Study, Annals of Medicine, 46:5, 324-329, DOI: 10.3109/07853890.2014.902226

To link to this article: https://doi.org/10.3109/07853890.2014.902226

ANN MED

informa
healthcare

Annals of Medicine, 2014; 46: 324–329

ISSN 0785-3890 print/ISSN 1365-2060 online
DOI: 10.3109/07853890.2014.902226

ORIGINAL ARTICLE

Sleep duration and insulin resistance in individuals without type 2 diabetes: The PPP-Botnia Study

Antti-Jussi Pyykkönen[1,2], Bo Isomaa[2,3], Anu-Katriina Pesonen[1], Johan G. Eriksson[2,4,5,6,7], Leif Groop[8,9], Tiinamaija Tuomi[2,10] & Katri Räikkönen[1]

[1]*Institute of Behavioural Sciences, University of Helsinki, Helsinki, Finland,* [2]*Folkhälsan Research Center, Helsinki, Finland,* [3]*Department of Social Services and Health Care, Jakobstad, Finland,* [4]*Department of General Practice and Primary Health Care, University of Helsinki, Helsinki, Finland,* [5]*National Institute for Health and Welfare, Helsinki, Finland,* [6]*Unit of General Practice, Helsinki University Central Hospital, Helsinki, Finland,* [7]*Vasa Central Hospital, Vasa, Finland,* [8]*Finnish Institute for Molecular Medicine (FIMM), University of Helsinki, Helsinki, Finland,* [9]*Department of Clinical Sciences—Diabetes & Endocrinology, Lund University, Malmö, Sweden, and* [10]*Department of Medicine, Helsinki University Central Hospital and Research Program for Diabetes and Obesity, University of Helsinki, Helsinki, Finland*

Introduction. **Both short and long sleep duration may increase risk of type 2 diabetes (diabetes). We studied if short and long sleep durations were associated with insulin resistance (IR) and insulin secretion in individuals without diabetes, and if the associations remained after we excluded individuals who reported more frequent and severe complaints of sleep apnea and insomnia.**
Participants and methods. **An oral glucose tolerance test (OGTT) was performed for 722 adults without diabetes. Indices of IR and insulin secretion were calculated. Sleep duration and complaints of sleep apnea and insomnia were self-reported.**
Results. **In comparison to average sleepers (6–9 h/night), short sleepers (< 6 h/night) had higher 120-min insulin and AUC glucose, and long sleepers (≥ 9 h/night) had higher fasting and 120-min insulin, 120-min glucose, and $HOMA_{IR}$ and lower Insulin Sensitivity Index. After adjusting for confounders and after excluding individuals who reported more frequent and severe complaints of sleep apnea and insomnia, long sleep duration remained significantly associated with IR and insulin secretion.**
Discussion. **Long but not short sleep duration is associated with IR and insulin secretion in individuals without diabetes whether or not accompanied by sleep complaints. Long sleepers may benefit from targeted preventions and interventions that aim at reducing risk of future diabetes.**

Key words: Insulin resistance, sleep complaints, sleep duration

Key messages

- Long but not short sleep duration is associated with insulin resistance in individuals without diabetes.
- This association is not explained by complaints of sleep apnea or insomnia, which may underlie variations in sleep duration.
- Individuals with long sleep duration may benefit from targeted preventions and interventions that that aim at reducing risk of future diabetes.

Introduction

Current prevalence and incidence rates of type 2 diabetes (diabetes) have exceeded the estimated rates projected for the future (1,2). At the same time, the number of individuals with sleep disorders, including sleep apnea and insomnia, and of those who report suffering from poor sleep quantity and quality, has been increasing (3). As sleep is considered a restorative process maintaining normal metabolic homeostasis, it is not surprising that sleep disorders and subjective complaints of poor sleep have been shown to confer a risk of diabetes (4–10).

Experimental sleep restriction studies in healthy young adults suggest that insulin resistance (IR) and impairments in insulin sensitivity and secretion, key features of diabetes, may mediate this link. In healthy men and women restriction of sleep to 4 hours for a single night was associated with increased IR and decreased insulin sensitivity during euglycemic clamp conditions (11). In healthy men restriction of sleep to 5 hours (12) and 4 hours (13) per night for one week was associated with decreased insulin sensitivity during euglycemic clamp conditions and intravenous glucose tolerance test (IVGTT) (12) and with reduced insulin secretion (12) and reduced glucose tolerance during an IVGTT (12,13).

The information provided by the experimental sleep restriction studies does not necessarily translate into natural environments where individuals differ significantly in their habitual sleep duration. Experimental sleep restriction studies do not provide information on the metabolic effects of long sleep duration either: both short and long sleep duration may be equally important vulnerability factors for future diabetes (10). Also, very few studies have tested if habitual sleep duration is associated with IR and insulin

Correspondence: Katri Räikkönen, Institute of Behavioural Sciences, University of Helsinki, PO Box 9 (Siltavuorenpenger 1 A), 00014 University of Helsinki, Finland. Fax: + 358-9-19129521. E-mail: katri.raikkonen@helsinki.fi

(Received 13 December 2013; accepted 3 March 2014)

secretion in individuals without diabetes (6,8,14,15). Finally, apart from sleep apnea and habitual snoring (6,8,15), the existing studies have rarely taken into account if individuals have a clinical diagnosis of insomnia or complain about it (6,8), a condition that may equally well underlie either short or long sleep duration. As a consequence, disentangling the effects of habitual sleep duration from underlying clinical diagnoses and/or subjective complaints becomes difficult.

We examined if short and long sleep durations were associated with indices of IR and insulin secretion in a sample of adult Finnish men and women participating in the population-based Prevalence, Prediction and Prevention of Diabetes (PPP-Botnia) Study (16–20). Our study contributes to the existing literature in the following ways. First, we tested the associations in men and women without known or newly diagnosed diabetes. Second, we carried out tests of these associations after we excluded participants who reported more frequent and severe complaints of sleep apnea and insomnia—factors that we have previously found to be associated with higher IR in the PPP-Botnia sample (16) and that may explain why sleep duration is either short or long. Finally, we tested if the associations were explained by a number of other important mediating and confounding factors including obesity and depressive symptoms, factors that are often characteristic of individuals who suffer from IR (18,21) and poor sleep quantity and quality (6,7,9,10).

Material and methods

Participants

The population-based PPP-Botnia Study in Finland has been described in detail previously (16–20). Of the 9,518 invited individuals, 5,208 (2,443 men and 2,765 women) (55%) participated in the study. Of those who participated, 2,232 were recruited from the study center in the town of Vasa. A psychological survey including questions on habitual sleep duration and complaints was added later to the study protocol and administered to 1,335 individuals of the Vasa subpopulation; 1,066 (79.9%) returned the questionnaire, with 958 (541 women and 417 men) providing complete data on self-reported sleep duration and complaints of sleep apnea and insomnia. Of them 97 using sleep medication and 7 who did not answer this question were excluded. An additional 41 individuals who had a previously and 21 who had a newly diagnosed diabetes and 70 who had incomplete data on IR were excluded. This resulted in a sample of 722 participants (400 women and 322 men) who had complete data on all study variables. These participants differed from the entire PPP-Botnia sample without diabetes ($n = 3{,}901$ after excluding 241 with previous/new diabetes) by being more frequently retired, they had higher fasting glucose, consumed more alcohol, reported regular exercise more frequently, and they were more insulin-resistant. All participants gave their written informed consent, and the study protocol was approved by the Ethics Committee of Helsinki University Central Hospital, Finland.

Insulin resistance and secretion

The subjects participated in an oral glucose tolerance test (OGTT) by ingesting 75 g of glucose after a 12-h overnight fast. During the OGTT, venous samples for plasma glucose and insulin were drawn at 0, 30, and 120 min. The homeostasis model assessment method ($HOMA_{IR}$) (22), Insulin Sensitivity Index (ISI) (23), Corrected Insulin Response (CIR) (24), and Disposition Index (DI) (25) were used as indices of IR and insulin secretion. The following formulas were used to calculate these variables: $HOMA_{IR}$ = fasting plasma insulin [mU/L] × fasting plasma glucose level [mmol/L]/22.5; ISI = 10,000/√ (fasting plasma glucose level [mmol/L] × fasting insulin [pmol/L]) × (mean OGTT glucose [mmol/L] × mean OGTT insulin [pmol/L]); CIR = (100 × insulin [pmol/L] at 30 min) / ((glucose [mmol/L] at 30 min) × (glucose [mmol/L] at 30 min–3.89 mmol/L)); DI = CIR × ISI. Area under the curve (AUC) of insulin and glucose were calculated as follow: AUC insulin = 15 × fasting plasma insulin [mU/L] + 15 × insulin [mU/L] at 30 min + 45 × insulin [mU/L] at 30 min + 45 × insulin [mU/L] at 120 min; AUC glucose = 15 × fasting plasma glucose + 15 × glucose [mmol/L] at 30 min + 45 × glucose [mmol/L] at 30 min + 45 × glucose [mmol/L] at 120 min.

Assays

Plasma glucose was measured with a glucose dehydrogenase method (HemoCue, Ängelholm, Sweden) and serum insulin by a fluoroimmunoassay (Delphia; Perkin-Elmer Finland, Turku, Finland).

Sleep duration

Self-reported sleep duration per night (hh:mm), over the past three months, was assessed with one question embedded in the Basic Nordic Sleep Questionnaire (BNSQ) (26). Individuals sleeping 6 hours or less and 9 hours or more were categorized as short and long sleepers, respectively (4–8,14); individuals sleeping >6 to <9 hours were categorized into the referent, average sleeper category.

Sleep complaints

The BNSQ also included questions on subjective complaints, over the past three months, of sleep apnea (frequency and quality of snoring, and frequency of breathing pauses) and insomnia (frequency of difficulties in falling asleep, maintaining sleep, and frequency of awakenings per one night). The questions were rated on a scale ranging from never or less than once per month (rated 1) to every day/night or almost every day/night per week (rated 5); except that, the quality of snoring was assessed using a scale ranging from 'I don't snore' (rated 1) to 'I snore very loudly and intermittently (there are silent breathing pauses when snoring is not heard and at times very loud snorts with gasping)' (rated 5), and frequency of awakenings during one night was assessed using a scale ranging from 'I do not wake up at night' (rated 1) to at least five times per night (rated 5).

We calculated two separate sum scores, one composed of answers to questions of sleep apnea and one composed of answers to questions of insomnia. On both sum scores the top quartile was used as a cut-off for identifying individuals with more frequent and severe sleep apnea and insomnia, respectively (16). Individuals with no or minor complaints of sleep apnea and insomnia scored below these cut-offs, respectively (16).

Mediating and confounding factors

Body weight and height were measured with subjects in light indoor clothing and without shoes. Body mass index was calculated as weight (kg) divided by height (m) squared. Waist circumference (cm) was measured by a research nurse with a soft tape on standing subjects midway between the lowest rib and the iliac crest. Depressive symptoms were self-rated using the Beck Depression Inventory II (27) (with scores 14 or above indicating at least mild symptomatology), and feelings of anxiety using the Spielberger Trait Anxiety Inventory (28). The participants also self-reported their weekly alcohol consumption (g/week), current smoking status (yes versus no or former smoker), occupational

status (categorized according to the classification system of Statistics Finland: manual workers, junior clericals, senior clericals, students, and retirees), and family history of known diabetes (yes versus no) in at least one first-degree relative (father, mother, or sibling). In addition, frequency and intensity of current physical activity and physical activity during the past 12 months were assessed using the validated Kuopio Ischemic Heart Disease Questionnaire (29). This questionnaire provides detailed information on common lifestyle, commuting, and leisure-time physical activity and enables assessment of total physical activity as metabolic equivalent (MET) hours per week (MET × hours/week). Based upon leisure-time activity, the participants were assigned into two groups: if they performed more than 30 minutes physical activity three or more times per week with an intensity resulting in breathlessness and/or sweating, they were assigned to regularly exercising group (yes), and if they performed less or performed no activity they were assigned to less/no exercising group (no).

Statistical analyses

First, we examined unadjusted mean differences between short and average sleepers and between long and average sleepers in fasting and 120-min glucose and insulin, area under the curve (AUC) of insulin and glucose, $HOMA_{IR}$, ISI, CIR, and DI by using independent samples *t* test. We then computed multiple linear regression analyses, with short and average sleep duration and long and average sleep duration as dichotomous independent variables in two separate models and indices of IR and insulin secretion as continuous outcome variables each tested in a separate model, to examine if these associations remained significant when we made adjustments for age and sex (Model 1) and further for the mediating and confounding factors (Model 2). To test if the expected associations between sleep duration and IR were independent of subjective sleep complaints, we re-ran the analyses first by excluding individuals who reported more severe and frequent complaints of sleep apnea and then by excluding individuals who reported more severe and frequent complaints of insomnia, and finally by excluding those who reported either or both complaints. Variables were log-transformed where appropriate. We used IBM SPSS 21 software to analyze the data.

Results

Characteristics of the study sample according to sleep duration per night are shown in Table I. In comparison to average sleepers, short sleepers had a higher BMI and a larger waist circumference, were older, more often smokers, and reported more frequent and severe complaints of insomnia. Long sleepers reported more often depressive symptoms of at least mild severity and reported less alcohol consumption. Both short and long sleepers less often worked in senior and junior clerical occupations. Of short, long, and average sleepers, respectively, 65, 12, and 154 reported more frequent and severe complaints of sleep apnea, insomnia, or both.

Table I shows unadjusted mean values of the indices of IR and insulin secretion according to sleep duration in the entire sample. In the unadjusted models, short sleepers had higher 120-min insulin, and long sleepers had higher fasting and 120-min insulin, higher $HOMA_{IR}$, and lower ISI than the average sleepers (Table I). When we made adjustment for age and sex (Model 1), only the associations of long sleep duration with fasting insulin, 120-min insulin, $HOMA_{IR}$, and ISI remained significant (Table I). Exclusion of individuals with more frequent and severe complaints of sleep apnea or insomnia, and individuals with either or both complaints, did not alter the significant associations, except that long sleep duration was no longer significantly associated with 120-min insulin (Table I).

Table I also shows that when we made adjustments for the other mediating and confounding factors (Model 2), short sleep duration was not significantly associated with any of the indices of IR and insulin secretion, while the association of long sleep duration with fasting insulin, $HOMA_{IR}$, and ISI remained statistically significant. We also computed a series of analyses to supplement these findings. When we replaced BMI with waist circumference the associations of long sleep duration with fasting insulin, $HOMA_{IR}$, and ISI did not change (P values < 0.05; data not shown). When we made adjustments for Spielberger Trait Anxiety Inventory score the significant associations of long sleep duration with fasting insulin, $HOMA_{IR}$, and ISI did not change either (P values < 0.05; data not shown).

Discussion

Our main finding is that while short sleep duration, namely sleeping 6 hours or less per night, was associated with higher glucose values during an OGTT in individuals without diabetes, this association was no longer statistically significant when we made adjustments for age and sex and the other mediating and confounding factors. Also, this association was not statistically significant in individuals who did not report more frequent and severe complaints of sleep apnea and insomnia. In contrast, long sleep duration, namely sleeping 9 hours or more per night, was associated with higher insulin and glucose values during an OGTT, and higher IR. These associations remained statistically significant when we made adjustments for age and sex and the mediating and confounding factors. The associations also remained statistically significant when we excluded individuals who reported more severe and frequent complaints of sleep apnea and insomnia. Our findings thus suggest that in individuals without diabetes, short sleep duration is not associated with IR and insulin secretion, while long sleep duration is, whether or not accompanied by more frequent and severe complaints of sleep apnea and insomnia.

Our findings add significantly to the previous literature which has suggested that both short and long sleep duration are associated with increased risk of diabetes and with higher IR in individuals without diabetes, though the findings are not entirely consistent (4–10,14,15). These studies have, however, not adequately controlled for sleep disorders or subjective complaints of sleep, above and beyond sleep apnea and habitual snoring (6,8,14,15). It remains unclear if some of the associations between short and long sleep duration with diabetes and IR are driven by potentially underlying sleep problems. Therefore, further studies are needed that will either confirm or refute our main findings.

Experimental sleep restriction studies may provide some insight into our null findings of short sleep duration and IR. Sleep restriction to 4–5 hours per night has been associated with higher IR in healthy individuals (11–13). Thus, the metabolic consequences of short sleep duration may be limited to conditions where the natural need for sleep is severely challenged. Short sleepers in our study reported more frequent and severe complaints of insomnia. This suggests that for some individuals in our sample short sleep duration reflected underlying sleep problems. For a subset of individuals, short sleep duration occurred without sleep complaints. For them, short sleep duration may be an intrinsic trait that is in concordance with their natural need of sleep. Hence, whether short sleep duration poses metabolic challenges in certain subgroups of individuals warrants further

Table I. Characteristics and mean values of insulin resistance indices and insulin secretion in average, short, and long sleepers.

	Sleep duration				
	Average (6–9 hours/night) (Referent) $n = 515$	Short ($\leq$ 6 hours/night) $n = 161$	*P* average versus Short	Long ($\geq$ 9 hours/night) $n = 46$	*P* average versus Long
Characteristic:	Mean $\pm$ SD/*n* (%)	Mean $\pm$ SD/*n* (%)		Mean $\pm$ SD/*n* (%)	
Age (years)	48.7 $\pm$ 14.5	51.6 $\pm$ 14.6	0.028	47.7 $\pm$ 16.8	0.642
Sex, women, *n* (%)	288 (55.9)	80 (49.7)	0.166	32 (69.6)	0.073
Family history for diabetes, first-grade yes, *n* (%)	139 (27.0)	42 (26.1)	0.821	8 (17.4)	0. 156
Current smoker, yes, *n* (%)	61 (11.9)	30 (18.8)	0.028	1 (2.2)	0.044
Regular exercise, yes, *n* (%)	321 (62.8)	87 (55.1)	0.081	32 (69.6)	0.363
Alcohol consumption, *n* (%)					
None	100 (19.4)	44 (27.3)	0.098	16 (34.8)	0.023
12–48 g/wk	254 (49.3)	70 (43.5)		22 (47.8)	
60 $\geq$ g/wk	161 (31.3)	47 (29.2)		8 (17.4)	
Occupational status, *n* (%)					
Senior clerical	137 (27.0)	28 (17.4)	0.005	7 (15.6)	0.008
Junior clerical	175 (34.4)	50 (31.1)		14 (31.1)	
Manual worker	71 (14.0)	31 (19.3)		4 (8.9)	
Retired	115 (22.6)	52 (32.3)		16 (35.6)	
Student	10 (2.0)	0 (0.0)		4 (8.9)	
Beck Depression Inventory (score $\geq$ 14), *n* (%)	32 (6.3)	14 (8.7)	0.289	7 (15.2)	0.023
Spielberger Trait Anxiety Inventory (score)[a]	36.3 $\pm$ 8.4	36.4 $\pm$ 8.6	0.972	38.3 $\pm$ 8.0	0.104
Weight (kg)	76.1 $\pm$ 14.3	78.5 $\pm$ 15.6	0.066	78.1 $\pm$ 16.7	0.364
Height (cm)	171.0 $\pm$ 9.6	170.2 $\pm$ 8.7	0.390	170.4 $\pm$ 8.8	0.703
Body mass index (kg/m^2)	25.9 $\pm$ 3.8	27.0 $\pm$ 4.8	0.003	26.8 $\pm$ 4.7	0.143
Waist circumference (cm)	87.7 $\pm$ 12.2	91.1 $\pm$ 12.7	0.002	88.2 $\pm$ 13.4	0.785
Sleep apnea, yes, *n* (%)	98 (21.5)	37 (28.0)	0.119	3 (8.1)	0.052
Insomnia, yes, *n* (%)	76 (17.6)	41 (30.1)	0.002	10 (22.7)	0.395
Sleep apnea and Insomnia, yes, *n* (%)	20 (3.9)	13 (8.1)	0.031	1 (2.2)	0.558
Napping, yes, *n* (%)	77 (15.0)	31 (19.3)	0.204	10 (21.7)	0.230
Insulin (mU/L)[a]					
Fasting	6.5 $\pm$ 6.2	6.7 $\pm$ 4.4	0.398	9.2 $\pm$ 7.8	0.001[bcdef]
120 minutes	29.7 $\pm$ 31.2	36.8 $\pm$ 39.2	0.026[e]	43.3 $\pm$ 48.2	0.032[b]
Area under the curve (mU/L/120-min)	4600.4 $\pm$ 3222.6	5034.9 $\pm$ 3160.9	0.072	5584.1 $\pm$ 4262.1	0.087
Glucose (mmol/L)[a]					
Fasting	5.5 $\pm$ 0.5	5.5 $\pm$ 0.5	0.911	5.6 $\pm$ 0.5	0.184
120 minutes	5.2 $\pm$ 1.4	5.5 $\pm$ 1.7	0.072	5.7 $\pm$ 1.5	0.053
Area under the curve (mmol/L/120-min)	823.9 $\pm$ 119.8	849.1 $\pm$ 133.5	0.031	841.5 $\pm$ 130.9	0.403
$HOMA_{IR}$[a]	1.6 $\pm$ 1.7	1.7 $\pm$ 1.1	0.406	2.4 $\pm$ 2.1	0.001[bcdef]
Insulin Sensitivity Index[a]	9.3 $\pm$ 4.9	8.7 $\pm$ 4.6	0.114	7.5 $\pm$ 4.4	0.004[bcdef]
Corrected Insulin Response[a]	155.0 $\pm$ 113.8	149.9 $\pm$ 110.4	0.622	169.1 $\pm$ 106.0	0.259
Disposition Index[a]	1248.1 $\pm$ 958.7	1146.6 $\pm$ 935.7	0.071	1164.3 $\pm$ 1131.5	0.179

[a]*P* values are derived from models where the values were log-transformed.
[b]Association remains statistically significant ($P < 0.05$) after controlling for age and sex (Model 1).
[c]Association remains statistically significant ($P < 0.05$) when participants with more severe and frequent complaints of sleep apnea were excluded.
[d]Association remains statistically significant ($P < 0.05$) when participants with more severe and frequent complaints of insomnia were excluded.
[e]Association remains statistically significant ($P < 0.05$) when participants with more severe and frequent complaints of sleep apnea, insomnia, or both, were excluded.
[f]Association remains statistically significant ($P < 0.05$) after controlling for age, sex, family history for diabetes, current smoking status, alcohol consumption, regular exercise, occupational status, body mass index, and depressive symptoms (Model 2).

studies. Our previous findings in this sample may offer further insight into this null association. We have previously shown that individuals who reported more frequent and severe complaints of sleep apnea and insomnia were more likely to be insulin resistant (16).

In our study long sleep duration was not associated with sleep apnea and insomnia. This may suggest that long sleep duration may not in our sample be a compensatory response to sleep problems. It is therefore not surprising that long sleep duration was associated with higher insulin values and IR even when we excluded those individuals who reported more frequent and severe complaints of sleep apnea and insomnia. Because our study design was cross-sectional we cannot rule out that, even in individuals without diabetes, long sleep duration may be a symptom resulting from altered insulin and glucose metabolism. This interpretation is in agreement with findings from one previous study suggesting that long sleep duration did not predict an increased risk of having impaired fasting glucose in individuals who at baseline had normal fasting glucose values (14). Clearly our findings warrant further longitudinal studies that allow testing for the direction of effects. Yet, a series of studies have demonstrated that long sleep duration increases the risk of future diabetes (10).

A further contribution of our study is that we were able to make adjustments for multiple factors that were expected either to mediate or confound the associations. When we made adjustments for age and sex the associations with short sleep duration were rendered non-significant while the associations with long sleep duration remained. When we made further adjustments for family history of diabetes, smoking, alcohol consumption, physical activity, occupation, obesity, waist circumference, depressive symptoms, and trait anxiety the associations of long sleep duration with IR and insulin secretion remained significant. These findings may suggest that the biological mechanisms underlying the associations between short and long sleep durations may differ, a suggestion also posed in other previous studies (10,14,15). The exact biological mechanisms remain elusive, however. Furthermore, even though sleep duration and IR have been linked with depressive symptoms in the previous studies by us (18,30–32) and

others (6,7,21), depressive symptoms did not provide mechanistic insight into the associations between sleep duration and IR and insulin secretion.

Strengths of this study lie in the population-based study design and detailed clinical examination. There are limitations to our study as well. Due to a cross-sectional study design we cannot draw causal inferences. A further limitation relates to generalizability from our findings beyond Caucasians. It is also noteworthy that we measured sleep duration and complaints using a self-reported, though validated questionnaire (26). This methodology differs from more objective measurement tools, such as actigraphy and polysomnography. There are advantages supporting the use of questionnaires in epidemiological study settings: they are cost-effective and easy to administer in larger populations. Validation studies do provide additional support for using questionnaire data in estimations of sleep duration and complaints (33). Finally, even though we were able to account for a number of mediators and confounders, our study did not provide diagnostic data on illnesses that may interfere with sleep, such as respiratory illnesses, or pain. Neither do our data offer detailed information on psychotropic medication use, such as use of hypnotics.

Our findings may have direct clinical relevance. While short sleep duration may not be significantly associated with indices of IR and insulin secretion in individuals without diabetes, long sleep duration may, whether or not it is accompanied by reports of more frequent and severe complaints of sleep apnea and insomnia. The group of long sleepers may benefit form targeted preventions and interventions that aim at reducing the risk of future diabetes.

Acknowledgements

The PPP-Botnia study has been financially supported by grants from the Finnish Academy (grant numbers 263401 & 267882), the Sigrid Juselius Foundation, Folkhälsan Research Foundation, Nordic Center of Excellence in Disease Genetics, Signe and Ane Gyllenberg Foundation, Swedish Cultural Foundation in Finland, Finnish Diabetes Research Foundation, Foundation for Life and Health in Finland, Finnish Medical Society, the Finnish Ministry of Education and Culture, the Paavo Nurmi Foundation, the Perklén Foundation, the Ollqvist Foundation, and the Närpes Health Care Foundation. The study has also been supported by the Municipal Health Care Center and Hospital in Jakobstad, and Health Care Centers in Vasa, Närpes, and Korsholm. The skilful assistance of the Botnia Study Group is gratefully acknowledged. National Doctoral Programme of Psychology.

Declaration of interest: The authors (A.-J.P.; A.-K.P.; K.R.; T.T.; L.G.) declare no conflict of interest. Johan G. Eriksson has been a consultant for and served on advisory boards for MSD, BMS, AstraZeneca, Roche, Eli Lilly and NovoNordisk. Bo Isomaa has received lecture fees from Boehringer-Ingelheim, MSD, NovoNordisk, and AstraZeneca.

References

1. International Diabetes Foundation. IDF Diabetes Atlas, 5th ed. Brussels, Belgium: International Diabetes Foundation; 2011.
2. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care. 2004;27:1047–53.
3. Roth T, Coulouvrat C, Hajak G, Lakoma MD, Sampson NA, Shahly V, et al. Prevalence and perceived health associated with insomnia based on DSM-IV-TR; International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; and Research Diagnostic Criteria/International Classification of Sleep Disorders, Second Edition criteria: results from the America Insomnia Survey. Biol Psychiatry. 2011;69:592–600.
4. Yaggi HK, Araujo AB, McKinlay JB. Sleep duration as a risk factor for the development of type 2 diabetes. Diabetes Care. 2006;29: 657–61.
5. Gangwisch JE, Heymsfield SB, Boden-Albala B, Buijs RM, Kreier F, Pickering TG, et al. Sleep duration as a risk factor for diabetes incidence in a large U.S. sample. Sleep. 2007;30:1667–73.
6. Gottlieb DJ, Punjabi NM, Newman AB, Resnick HE, Redline S, Baldwin CM, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med. 2005;165:863–7.
7. Ayas NT, White DP, Al-Delaimy WK, Manson JE, Stampfer MJ, Speizer FE, et al. A prospective study of self-reported sleep duration and incident diabetes in women. Diabetes Care. 2003;26:380–4.
8. Chao CY, Wu JS, Yang YC, Shih CC, Wang RH, Lu FH, et al. Sleep duration is a potential risk factor for newly diagnosed type 2 diabetes mellitus. Metabolism. 2011;60:799–804.
9. Mallon L, Broman JE, Hetta J. High incidence of diabetes in men with sleep complaints or short sleep duration: a 12-year follow-up study of a middle-aged population. Diabetes Care. 2005;28:2762–7.
10. Cappuccio FP, D'Elia L, Strazzullo P, Miller MA. Quantity and quality of sleep and incidence of type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2010;33:414–20.
11. 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. J Clin Endocrinol Metab. 2010;95:2963–8.
12. 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.
13. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet. 1999;354:1435–9.
14. Rafalson L, Donahue RP, Stranges S, Lamonte MJ, Dmochowski J, Dorn J, et al. Short sleep duration is associated with the development of impaired fasting glucose: the Western New York Health Study. Ann Epidemiol. 2010;20:883–9.
15. Liu R, Zee PC, Chervin RD, Arguelles LM, Birne J, Zhang S, et al. Short sleep duration is associated with insulin resistance independent of adiposity in Chinese adult twins. Sleep Med. 2011;12:914–19.
16. Pyykkönen AJ, Isomaa B, Pesonen AK, Eriksson JG, Groop L, Tuomi T, et al. Subjective sleep complaints are associated with insulin resistance in individuals without diabetes: the PPP-Botnia Study. Diabetes Care. 2012;35:2271–8.
17. Pyykkönen AJ, Räikkönen K, Tuomi T, Eriksson JG, Groop L, Isomaa B. Association between depressive symptoms and metabolic syndrome is not explained by antidepressant medication: results from the PPP-Botnia Study. Ann Med. 2012;44:279–88.
18. Pyykkönen AJ, Räikkönen K, Tuomi T, Eriksson JG, Groop L, Isomaa B. Depressive symptoms, antidepressant medication use, and insulin resistance: the PPP-Botnia Study. Diabetes Care. 2011; 34:2545–7.
19. Pyykkönen AJ, Räikkonen K, Tuomi T, Eriksson JG, Groop L, Isomaa B. Stressful life events and the metabolic syndrome: the prevalence, prediction and prevention of diabetes (PPP)-Botnia Study. Diabetes Care. 2010;33:378–84.
20. Isomaa B, Forsen B, Lahti K, Holmstrom N, Waden J, Matintupa O, et al. A family history of diabetes is associated with reduced physical fitness in the Prevalence, Prediction and Prevention of Diabetes (PPP)-Botnia study. Diabetologia. 2010;53:1709–13.
21. Silva N, Atlantis E, Ismail K. A review of the association between depression and insulin resistance: pitfalls of secondary analyses or a promising new approach to prevention of type 2 diabetes? Curr Psychiatry Rep. 2012;14:8–14.
22. Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia. 1985;28:412–19.
23. Bergman RN, Prager R, Volund A, Olefsky JM. Equivalence of the insulin sensitivity index in man derived by the minimal model method and the euglycemic glucose clamp. J Clin Invest. 1987;79:790–800.
24. Hanson RL, Pratley RE, Bogardus C, Narayan KM, Roumain JM, Imperatore G, et al. Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol. 2000;151:190–8.
25. Bergman RN, Ader M, Huecking K, Van Citters G. Accurate assessment of beta-cell function: the hyperbolic correction. Diabetes. 2002;51 (Suppl 1):S212–20.

26. Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. J Sleep Res. 1995;4(S1):150–5.
27. Beck AT, Steer RA, Ball R, Ranieri W. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. J Pers Assess. 1996;67:588–97.
28. Spielberger C, Gorsuch R, Lushene R, Vagg P, Jacobs G. Manual for the State-Trait Anxiety Inventory. Palo Alto, CA: Consulting Psychologists Press; 1983.
29. Salonen JT, Lakka TA. Assessment of physical activity in population studies–validity and consistency of the methods in the Kuopio Ischemic Heart Disease Risk Factor Study. Scand J Sports Sci. 1987;9:89–95.
30. Pesonen AK, Kajantie E, Heinonen K, Pyhala R, Lahti J, Jones A, et al. Sex-specific associations between sleep problems and hypothalamic-pituitary-adrenocortical axis activity in children. Psychoneuroendocrinology. 2012;37:238–48.
31. Paavonen EJ, Strang-Karlsson S, Räikkönen K, Heinonen K, Pesonen AK, Hovi P, et al. Very low birth weight increases risk for sleep-disordered breathing in young adulthood: the Helsinki Study of Very Low Birth Weight Adults. Pediatrics. 2007;120:778–84.
32. Räikkönen K, Matthews KA, Kuller LH. Depressive symptoms and stressful life events predict metabolic syndrome among middle-aged women: a comparison of World Health Organization, Adult Treatment Panel III, and International Diabetes Foundation definitions. Diabetes Care. 2007;30:872–7.
33. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? Epidemiology. 2008;19:838–45.