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Associations between Poor Sleep and Glucose Intolerance in Prediabetes

Ibasaraboh D. Iyegha, **Angela Y. Chieh**, **Bianca M. Bryant**, **Li Li***

Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, Birmingham, AL, 35294

Abstract

Objectives—A cross-sectional study was designed to investigate the association between sleep quality and glucose metabolism among people with prediabetes, and to explore the potential pathways linking poor sleep to glucose intolerance.

Methods—One hundred fifty-five females and males, Caucasians and African Americans, aged 19–70 completed the study for data analysis. All participants were assessed for sleep quality using the Pittsburgh Sleep Quality Index (PSQI). Fasting glucose and 2-h glucose levels were collected via a 2-h oral glucose tolerance test (OGTT) and used to define prediabetes. Participants provided blood samples for measuring inflammatory markers. Associations were conducted using Pearson's correlation with adjustments for gender, age, and body mass index (BMI). Analysis of covariance (ANCOVA) was applied to compare the two groups, prediabetes group versus the control group, after controlling for gender, age, and BMI. Regression was used to investigate predictive power of sleep subscales for inflammatory factors and glucose levels.

Results—More people with prediabetes suffered from poor sleep than in the normal glucose group (62% vs. 46%). The OGTT measures, i.e. fasting glucose and 2-h glucose levels, correlated with PSQI measures, but these associations did not maintain statistical significance after adjusting for gender, age, and BMI. The C-reactive protein (CRP) levels were greater in the prediabetes group than the normal glucose group (0.37±.07 vs. 0.18±0.06 mg/L). Additionally, there was a positive correlation between sleep disturbance and CRP levels (r=0.30, p=0.04). Regression analysis found that sleep disturbance predicted CRP levels and significance remained after adding covariates (β=0.20, p=0.04). No significant difference was observed in other measured inflammatory factors, including interleukin (IL)-6, IL-8, IL-10 and tumor necrosis factor alpha (TNFα), between the two groups.

***Corresponding author** Li Li, M.D; Ph.D., Department of Psychiatry and Behavioral Neurobiology, University of Alabama at Birmingham, 1720 University Blvd., Birmingham, AL, 35294, Phone: (205) 934-6269, Fax: (205) 975-4462, liyli@uabmc.edu.

6. Author contributions

I.I. collected and analyzed the data, drafted, edited and approved the final manuscript. B.B. drafted, edited and approved the final manuscript. A.C. analyzed the data, edited and approved the final manuscript. L.L. conceptualized and designed the study, analyzed the data, reviewed, edited and approved the final manuscript.

Conflict of Interest

The authors report no conflicts of interest in this work.

Conclusion—Prediabetes is positively associated with poor sleep. Increased CRP levels may be a potential underlying mechanism of this association between prediabetes and poor sleep which warrants further study. Our findings highlight the importance for clinicians to evaluate sleep quality as part of preventing the onset of future diabetes in this particular population.

Precis

The relationship between sleep quality and prediabetes was investigated. Poor sleep quality was related to prediabetes. Increased inflammatory factors may mediate this relationship.

Keywords

Prediabetes; poor sleep; glucose intolerance; inflammatory factors

1. Introduction

Sleep is an essential biological process for health and has a major role in regulating glucose metabolism and other physiological functions, with sleep disturbance having negative health outcomes (Qian and Scheer, 2016; Scott, 1989) (Anothaisintawee et al., 2016). The prevalence of sleep disturbances has been on the rise in the past few decades, and poor sleep quality has increasingly been recognized as a risk factor for poor health outcomes such as obesity, diabetes and cardiovascular diseases (Liu et al., 2017; Reutrakul and Van Cauter, 2014; Sweatt et al., 2018). Epidemiological studies have shown that short sleep duration in adolescents and adults is associated with excessive body fat (Taheri, 2006). The risk of developing Type 2 diabetes (T2D) in those with sleep disturbances has also been studied, with increased risk associated with both sleep quantity (sleep duration less than 5h or more than 9h) and sleep quality (difficulty in initiating or maintaining sleep) (Shan et al., 2015; Yadav and Cho, 2018). Moreover, both sleep quantity and sleep quality are associated with poor glycemic control in patients with T2D (Lee et al., 2017; Zhu et al., 2017).

Prediabetes is a risk factor for the development of T2D and cardiovascular diseases (Buysschaert et al., 2015; Tabak et al., 2012). Per 2018 American Diabetes Association criteria, fasting plasma glucose, 2-h plasma glucose during 75-g oral glucose tolerance test (OGTT), and hemoglobin A1C are equally appropriate to test for prediabetes (2018). Prediabetes has been increasing in prevalence in the past years, and 5–10% of people with prediabetes progress to diabetes annually (Tabak et al., 2012). Short sleep duration increases the risk for this progression, serving as a potential modifiable risk factor (Kowall et al., 2016). Studies in adults show that partial and total sleep deprivation could lead to glucose intolerance and insulin resistance even in healthy volunteers (Reynolds et al., 2012; Spiegel et al., 1999). The associations between sleep quality, sleep duration and prediabetes are also suggested, however, there is much less literature available with inconsistent reports (Engeda et al., 2013; Kim et al., 2017; Rafalson et al., 2010). Another limitation of the previous studies is that their definition of prediabetes is based on self report, raising the possibility that undiagnosed cases of prediabetes may not be included in the study outcomes. This limitation can be significant because per the CDC, an estimated 33.9% of U.S. adults aged 18 years or older (~84.1 million people) had prediabetes in 2015 based on their fasting glucose or A1C level (CDC). Therefore, more accurate measures are warranted to determine

the relationship between prediabetes and sleep disturbances, including sleep quantity and sleep quality.

Although studies have suggested an association between poor sleep quality and prediabetes, the mechanisms that increase the risk for prediabetes and subsequent development of T2D in those with poor sleep remain unclear. Increased levels of inflammatory factors may be a potential pathway linking poor sleep to prediabetes. A meta-analysis showed that poor sleep is associated with increased inflammatory factors such as C-reactive protein (CRP) and interleukin (IL)-6 but not tumor necrosis factor-α (TNFα) (Irwin et al., 2016). However, some studies found TNFα to be elevated with short sleep durations (Patel et al., 2009). One explanation might be due to how sleep duration was assessed in the individual studies. *For example, Patel et al study used polysomnography to measure sleep duration, and reported an association between TNFα and short sleep duration (Patel et al., 2009). In contrast, other studies used self-reported questionnaires to assess sleep duration but did not find TNFα was associated with short sleep duration* (Irwin et al., 2016). In addition, other studies found elevated CRP levels to be limited to either males or females with sleep disturbances suggesting that there is more complexity to these associations (Liu et al., 2014; Richardson and Churilla, 2017). Inflammatory factors such as TNFα and IL-6 have already been implicated in the development of insulin resistance, an important factor in the pathogenesis of prediabetes and diabetes (Akash et al., 2018; Li and Messina, 2009). Thus, there is potential for these inflammatory factors to play a role in the pathway linking poor sleep to glucose intolerance and prediabetes.

Because of heterogeneous results and limitations of previous studies regarding the association between poor sleep and prediabetes, as well as the lack of underlying mechanisms, a cross-sectional study was conducted. The aim of the current study was to investigate this relationship and to explore the potential mechanisms underlying their association by studying the inflammatory factors in an adult population.

2. Methods

2.1 Participants

This was a cross-sectional study design. All participants were recruited in the local communities surrounding Birmingham, AL, from October 2014 to December 2018. The project was approved by the University of Alabama at Birmingham Institutional Review Board and was conducted in accordance with the Helsinki Declaration of 1975. All participants provided written informed consent prior to participating in any research procedures. Participants included men and women between ages of 19–70 years old. Participants were excluded if they: (1) had a diagnosis of diabetes; (2) were taking medications or using alcohol or substances known to affect glucose metabolism and insulin sensitivity; (3) were pregnant or lactating; (4) had a diagnosis of sleep disorders, including sleep apnea; or (5) had a diagnosis of immune system disorders and/or were taking antibiotics in the last 30 days. Demographic data, medical history, and medications were collected by self-report (Table 1). Body mass index (BMI) was calculated using the Quetelet index (kg/m^2). Since sleep problem is a core symptom in depression, depression in all

participants was measured using the Beck Depression Inventory, which was designed to assess the severity of depressive symptoms by self-report (Richter et al., 1998).

2.2 Measures for sleep quality

The Pittsburgh Sleep Quality Index (PSQI) was developed for use in the clinical assessment of sleep quality and is a validated measure of habitual sleep quality over a 1-month time interval. The PSQI includes a 19-item self-rated questionnaire and measures sleep quality along seven dimensions, including 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep disturbance; 6) use of sleeping medications; and 7) daytime dysfunction over the last month (Buysse et al., 1989). Each dimension is rated on a four-point Likert scale (i.e. 0–3). Scores from these dimensions are added together to generate a global score ranging from 0 to 21. Greater PSQI scores indicate worse sleep quality while a score of ≥ 5 indicates poor sleep quality (Akash et al., 2018; Buysse et al., 1989).

2.3 Definition of prediabetes using the oral glucose tolerance test

After fasting for at least 10–12 h, a 2-h OGTT with the ingestion of 75g of oral glucose was performed in each participant (Weyer et al., 1999). Plasma glucose was measured by the glucose oxidase method using a glucose analyzer (Beckman Coulter Unicell DxC 800). Incremental area under the curve (AUC) for plasma glucose levels throughout the OGTT was calculated using the trapezoidal rule. In the current study, the definition based on 2018 American Diabetes Association criteria, prediabetes refers to fasting plasma glucose 100–125 mg/dl, and/or 2-h plasma glucose from OGTT at 140–199 mg/dl (2018).

2.4 Blood collection and serum measurements

Fifteen milliliters of peripheral blood samples were obtained by venipuncture from each participant *who presented to the laboratory without fasting*. Blood samples were centrifuged at 3000g for 10 mins. The samples were immediately divided into aliquots and frozen at −80°C until further analysis. Participants were not requested to fast before blood collection. The analysis for inflammatory factors, including IL-6, IL-8, IL-10, CRP, and TNFα, were performed using a Meso Scale Discovery multiplex assay and analyzed with MPSQ Discovery Workbench software (Gaithersburg, MD). Concentrations for inflammatory factors were expressed in pg/ml except CRP in mg/L. Each sample was run in duplicate, and the mean of the duplicate samples was reported. For these assays, duplicate readings were performed on a subset of samples to demonstrate a high level of correlation between measurements; intra-class correction varied between 0.95 and 1.0 ($p<0.001$).

2.5 Statistical analysis

All analyses were conducted using the Statistical Package for the Social Sciences, version 24 (Chicago, IL), and p value was set at <0.05 as significant. All variables were tested for normality of distribution and would be natural log-transformed prior to data analysis if needed. Continuous data are presented as means (±standard error). Differences between the two groups in variables of interest were compared using Chi-square test for categorical data, including gender, race, education levels and employment status, and using independent T-

test for continuous data, including age and BMI. Partial Pearson correlation analysis was used to determine the relationship between PSQI global score, PSQI subscales, and inflammatory factors with age, gender, and BMI as covariates in all models. Analysis of covariance (ANCOVA) adjusted for age, gender, and BMI was used to determine differences in outcome variables between the two groups. Additionally, regression was used to further investigate predictive power of sleep subscales so that correlational results would be supplemented. Two regression models were created, the first without fixed covariates and the second with fixed covariates for age, gender, and BMI. The first regression used stepwise procedure to enter variables from a list of age, gender, BMI, sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep meds, and daytime dysfunction. Criteria were 0.05 for entry and 0.1 for removal. This method allowed for the creation of a model that best predicted the outcome. However, because some important variables such as age, gender, and BMI may not be included because they are not significant predictors, the second regression tested the inclusion of those three variables as necessary covariates. For the second regression, age, gender, and BMI were entered into the model and could not be removed. The seven sleep subscale variables were then entered in a stepwise procedure using the same criteria for entry and removal. These models were created for inflammatory factors and glucose levels, including CRP, IL-6, IL-8, IL-10, TNFa, fasting glucose and 2-h glucose. All predictors listed as significant were significant to an alpha level of 0.05.

3. Results

3.1 Participant Characteristics

A total of 188 participants were enrolled in the study, and 155 participants completed the study for data analysis. Of the 33 subjects that were excluded, 24 subjects did not complete the OGTT, 4 were excluded for incidental diabetes, and 5 refused the blood draw. According to the American Diabetes Association diagnostic criteria for prediabetes, participants were stratified into a normal glucose tolerance group (NGT, n=95) and prediabetes group (prediabetes, n=60) (2014; 2018). Of those in the prediabetes group, approximately 71% were diagnosed by FPG, 7% by 2-hr glucose, and 22% by both FPG and 2-hr glucose. As shown in Table 1, participants in the prediabetes group tended to be older than in NGT group (41.0±1.7 vs. 36.0±1.2 years), and there were more female participants in the NGT group than in the prediabetes group. However, there was no significant difference between the groups in race, education level, employment status, and BMI. Blood pressure levels (i.e. systolic blood pressure and diastolic blood pressure), and depressive score using the Beck Depression Inventory did not differ between the two groups. Therefore, gender and age were included as covariates for all data analysis. Our prior study indicates that BMI is related to chronic inflammatory status, thus BMI was controlled in all data analyses (Li et al., 2015; Shelton et al., 2015).

3.2 Association between OGTT measures and PSQI measures

Global PSQI scores and subscales of PSQI were compared between the two groups, and no significant differences were observed (Table 2). However, more participants had poor sleep quality in the prediabetes group compared with the NGT group although not significant

(62% vs. 46%, p=0.09). Partial Pearson's correlation was conducted between the OGTT measurements and PSQI global score and subscales in participants with prediabetes (Table 3). As shown in Table 3, fasting glucose, 2-h glucose and glucose AUC had positive associations with global PSQI score and many of the PSQI subscales. After controlling for gender, age, and BMI, these associations remained but were not statistically significant. Stepwise regression analysis in the prediabetes group found consistent results to correlational analysis. For fasting glucose, BMI and sleep disturbance remained the only two significant predictors retained in the model (β=2.24, p=0.03). For the 2-h glucose, sleep disturbance was the only significant predictor (β=11.67, p=0.02). However, upon fixing the covariates BMI, age, and gender, sleep disturbance was no longer significant for either OGTT measure. No other sleep subscales were found to predict OGTT outcomes.

3.3 Association between the inflammatory factors and PSQI measures

Comparisons of the inflammatory factors, including CRP, IL-6, IL-8, IL-10 and TNFα, were performed between the two groups (Table 4). Levels of all inflammatory factors were converted to their log10 values to reach normal distribution. The CRP levels in the prediabetes group were significantly greater than the NGT group (0.37±0.07 vs. 0.18±0.06mg/L, p=0.03) after controlling for gender, age, and BMI. However, there was no significant difference in levels of IL-6, IL-8, IL-10, and TNFα between the two groups when gender, age and BMI were adjusted. The inflammatory factors were also correlated with the PSQI subscales in participants with prediabetes (Table 5). After controlling for gender, age, and BMI, only the association between sleep disturbance and CRP remained statistically significant (r=0.30, p=0.04). Stepwise regression analysis found that sleep disturbance was a significant predictor of CRP (β=0.24, p=0.008) in the prediabetes group. Even with the addition of covariates age, gender and BMI, sleep disturbance remained predictive of CRP level (β=0.20, p=0.04). Sleep subscales were not found to significantly predict other inflammatory factors.

4. Discussion

In the current study, our data suggests that those with prediabetes tend to have poor sleep, which is related to glucose intolerance as demonstrated by the associations between OGTT measures and PSQI measures independently of gender, age and BMI. Additionally, in those with prediabetes, sleep disturbance was positively associated with CRP, which was significantly greater in the prediabetes group in comparison to those with normal glucose tolerance after controlling for gender, age, and BMI. In contrast, we did not observe differences in levels of IL-6, IL-8, IL-10, or TNFα between the two groups. This finding expands our understanding of the associations between prediabetes and poor sleep, and the potential underlying pathways.

A number of previous studies have examined whether there is a link between poor sleep quality and prediabetes, but the results have been inconsistent. Variations in the criteria used to define prediabetes, controlling for BMI of the study populations, and the measure for sleep quality may partly explain this inconsistency. For instance, the outcomes of most studies in the literature were ascertained through self report of prediabetes, which may have

resulted in bias. Just a few studies measured fasting blood glucose levels (Engeda et al., 2013; Kim et al., 2017; Rafalson et al., 2010). It is reported that prediabetes is underdiagnosed although the prevalence is as high as 33.9% in adults in the general population (CDC). In the present study, the measurement of both fasting glucose and 2-hr glucose levels in the OGTT to define prediabetes probably produced less-biased estimates. In addition, few studies evaluated this association with adjusting for BMI, although BMI is known to be related with poor sleep (Jennings et al., 2007; Sweatt et al., 2018). Many of previous studies evaluated sleep quality with only simple questions rather than a standardized and complete assessment questionnaire. In contrast, in this study, we used the validated PSQI questionnaire to measure sleep quality comprehensively because it allowed us to evaluate different aspects of sleep quality (Buysse et al., 1989).

Our results found that several aspects in the PSQI are associated with impaired glucose tolerance and impaired fasting glucose, corroborating the results of prior study findings and meta-analyses of prospective studies. Our observation is consistent with a study in a Chinese population in which Hung, et al, found that impaired glucose tolerance was significantly associated with poor sleep quality, which was independent of cardio-metabolic risk factors (Hung et al., 2013). Furthermore, previous studies observed a detrimental impact of sleep deprivation on glucose metabolism in response to a glucose challenge (Liu et al., 2017; Spiegel et al., 1999). Thus, it is speculated that the effects of poor sleep quality on glucose metabolism may be detected only after a glucose load. Furthermore, associations between PSQI and glucose levels remained but not significantly after age, gender and BMI were controlled, indicative of the importance of considering other risk factors for prediabetes when the relationship is studied. However, further studies are warranted to confirm the results in a larger population and to expand the observations in other ethnicities.

There are several possible mechanisms underlying the association between poor sleep and prediabetes. Our mechanistic study revealed that CRP was significantly greater in participants with prediabetes compared to controls. This is supportive of a possible role of chronic inflammation as an intermediate between poor sleep and prediabetes. The current study is partially consistent with a recent meta-analysis of 72 studies evaluating associations between sleep disturbance, CRP, IL-6, and TNFα in that sleep disturbance was found to be associated with increased CRP and IL-6. However, our results showed that IL-6 had no association with the PSQI global score and subscales. One potential explanation for heterogeneous results could be related to BMI. We adjusted BMI when data was analyzed since greater BMI is known to be associated with chronic low-grade inflammation, and controlling for BMI might attenuate the association between IL-6 and poor sleep quality (Popko et al., 2010; Sweatt et al., 2018). Indeed, our current study found that IL-6 was associated with global PSQI ($r=0.21$, $p=0.15$), sleep quality ($r=0.24$, $p=0.10$), sleep disturbance ($r=0.18$, $p=0.23$), and use of sleep meds ($r=0.26$, $p=0.08$), but correlation did not remain after BMI was adjusted.

The increasing prevalence of prediabetes and the risk of subsequent diabetes highlight the importance of studies focusing on predictors for prediabetes. Lifestyle is important to prevent and reduce the risk for prediabetes and subsequent diabetes. The linkage between poor sleep and prediabetes suggests that lifestyle modification, i.e. improving sleep quality,

might be another strategy to decrease the rate of onset of diabetes in individuals with prediabetes. Our data provides further evidence for the prevention of diabetes at the population level, given the poor sleep quality is highly prevalent (Jean-Louis et al., 2014; Jennings et al., 2007). In particular, the current study found that several sleep aspects in the PSQI are associated with glucose intolerance in prediabetic participants, indicating that clinicians might be able to use this particular sleep questionnaire to assess their prediabetic patients' susceptibility to developing future diabetes. Future research implementing preventative interventions to improve sleep quality in prediabetic individuals could potentially alleviate the progression to diabetes. Strategies of improving sleep quality could decrease the outcome of prediabetes along with other adverse health outcomes.

Several limitations of the present study should be considered when interpreting the results. First, the assessment of sleep quality was based on a validated but self-reported questionnaire, which is reported to correlate modestly with objective measures of sleep duration (Buysse et al., 1989). Second, many participants in the present study were highly educated adults; thus, caution should be taken when generalizing the present study findings to other populations. Third, due to the nature of a cross-sectional design, a cause and effect relationship between poor sleep and prediabetes could not be established.

In conclusion, this study suggested that poor sleep is associated with glucose intolerance in prediabetic individuals. CRP levels among participants with prediabetes indicate that elevated CRP is related to poor sleep. Further investigation into a cause and effect relationship between poor sleep and prediabetes will lead to a better understanding of the impact of poor sleep quality on prediabetes and subsequent diabetes. Our findings suggest that sufficient sleep quality is important for delaying or preventing the progression of prediabetes to diabetes.

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References

https://www.cdc.gov/diabetes/data/statistics-report/prevalence.html

2014 Diagnosis and classification of diabetes mellitus. Diabetes care 37 Suppl 1, S81–90. [PubMed: 24357215]

2018 Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes care 41, S13–s27. [PubMed: 29222373]

Akash MSH, Rehman K, Liaqat A, 2018 Tumor Necrosis Factor-Alpha: Role in Development of Insulin Resistance and Pathogenesis of Type 2 Diabetes Mellitus. Journal of cellular biochemistry 119, 105–110. [PubMed: 28569437]

Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A, 2016 Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis. Sleep medicine reviews 30, 11–24. [PubMed: 26687279]

Buysschaert M, Medina JL, Bergman M, Shah A, Lonier J, 2015 Prediabetes and associated disorders. Endocrine 48, 371–393. [PubMed: 25294012]

Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ, 1989 The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry research 28, 193–213. [PubMed: 2748771]

Engeda J, Mezuk B, Ratliff S, Ning Y, 2013 Association between duration and quality of sleep and the risk of pre-diabetes: evidence from NHANES. Diabetic medicine : a journal of the British Diabetic Association 30, 676–680. [PubMed: 23425048]

Hung HC, Yang YC, Ou HY, Wu JS, Lu FH, Chang CJ, 2013 The relationship between impaired fasting glucose and self-reported sleep quality in a Chinese population. Clinical endocrinology 78, 518–524. [PubMed: 22548278]

Irwin MR, Olmstead R, Carroll JE, 2016 Sleep Disturbance, Sleep Duration, and Inflammation: A Systematic Review and Meta-Analysis of Cohort Studies and Experimental Sleep Deprivation. Biological psychiatry 80, 40–52. [PubMed: 26140821]

Jean-Louis G, Williams NJ, Sarpong D, Pandey A, Youngstedt S, Zizi F, Ogedegbe G, 2014 Associations between inadequate sleep and obesity in the US adult population: analysis of the national health interview survey (1977-2009). BMC public health 14, 290. [PubMed: 24678583]

Jennings JR, Muldoon MF, Hall M, Buysse DJ, Manuck SB, 2007 Self-reported sleep quality is associated with the metabolic syndrome. Sleep 30, 219–223. [PubMed: 17326548]

Kim CW, Chang Y, Sung E, Ryu S, 2017 Sleep duration and progression to diabetes in people with prediabetes defined by HbA1c concentration. Diabetic medicine : a journal of the British Diabetic Association 34, 1591–1598. [PubMed: 28734090]

Kowall B, Lehnich AT, Strucksberg KH, Fuhrer D, Erbel R, Jankovic N, Moebus S, Jockel KH, Stang A, 2016 Associations among sleep disturbances, nocturnal sleep duration, daytime napping, and incident prediabetes and type 2 diabetes: the Heinz Nixdorf Recall Study. Sleep medicine 21, 35–41. [PubMed: 27448469]

Lee SWH, Ng KY, Chin WK, 2017 The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: A systematic review and meta-analysis. Sleep medicine reviews 31, 91–101. [PubMed: 26944909]

Li L, Chassan RA, Bruer EH, Gower BA, Shelton RC, 2015 Childhood maltreatment increases the risk for visceral obesity. Obesity (Silver Spring, Md.) 23, 1625–1632. [PubMed: 26146933]

Li L, Messina JL, 2009 Acute insulin resistance following injury. Trends in endocrinology and metabolism: TEM 20, 429–435. [PubMed: 19800814]

Liu R, Liu X, Zee PC, Hou L, Zheng Z, Wei Y, Du J, 2014 Association between sleep quality and C-reactive protein: results from national health and nutrition examination survey, 2005–2008. PloS one 9, e92607. [PubMed: 24663098]

Liu TZ, Xu C, Rota M, Cai H, Zhang C, Shi MJ, Yuan RX, Weng H, Meng XY, Kwong JS, Sun X, 2017 Sleep duration and risk of all-cause mortality: A flexible, non-linear, meta-regression of 40 prospective cohort studies. Sleep medicine reviews 32, 28–36. [PubMed: 27067616]

Patel SR, Zhu X, Storfer-Isser A, Mehra R, Jenny NS, Tracy R, Redline S, 2009 Sleep duration and biomarkers of inflammation. Sleep 32, 200–204. [PubMed: 19238807]

Popko K, Gorska E, Stelmaszczyk-Emmel A, Plywaczewski R, Stoklosa A, Gorecka D, Pyrzak B, Demkow U, 2010 Proinflammatory cytokines Il-6 and TNF-alpha and the development of inflammation in obese subjects. European journal of medical research 15 Suppl 2, 120–122. [PubMed: 21147638]

Qian J, Scheer F, 2016 Circadian System and Glucose Metabolism: Implications for Physiology and Disease. Trends in endocrinology and metabolism: TEM 27, 282–293. 173. [PubMed: 27079518]

Rafalson L, Donahue RP, Stranges S, Lamonte MJ, Dmochowski J, Dorn J, Trevisan M, 2010 Short sleep duration is associated with the development of impaired fasting glucose: the Western New York Health Study. Annals of epidemiology 20, 883–889. [PubMed: 20620078]

Reutrakul S, Van Cauter E, 2014 Interactions between sleep, circadian function, and glucose metabolism: implications for risk and severity of diabetes. Annals of the New York Academy of Sciences 1311, 151–173. [PubMed: 24628249]

Reynolds AC, Dorrian J, Liu PY, Van Dongen HP, Wittert GA, Harmer LJ, Banks S, 2012 Impact of five nights of sleep restriction on glucose metabolism, leptin and testosterone in young adult men. PloS one 7, e41218. [PubMed: 22844441]

Richardson MR, Churilla JR, 2017 Sleep Duration and C-Reactive Protein in US Adults. Southern medical journal 110, 314–317. [PubMed: 28376532]

Richter P, Werner J, Heerlein A, Kraus A, Sauer H, 1998 On the validity of the Beck Depression Inventory. A review. Psychopathology 31, 160–168. [PubMed: 9636945]

Scott EM, 1989 Hypnosis: emotions for the tin man (the schizoid personality). The American journal of clinical hypnosis 31, 204–208. [PubMed: 2919575]

Shan Z, Ma H, Xie M, Yan P, Guo Y, Bao W, Rong Y, Jackson CL, Hu FB, Liu L, 2015 Sleep duration and risk of type 2 diabetes: a meta-analysis of prospective studies. Diabetes care 38, 529–537. [PubMed: 25715415]

Shelton RC, Falola M, Li L, Zajecka J, Fava M, Papakostas GI, 2015 The pro-inflammatory profile of depressed patients is (partly) related to obesity. Journal of psychiatric research 70, 91–97. [PubMed: 26424427]

Spiegel K, Leproult R, Van Cauter E, 1999 Impact of sleep debt on metabolic and endocrine function. Lancet (London, England) 354, 1435–1439.

Sweatt SK, Gower BA, Chieh AY, Liu Y, Li L, 2018 Sleep quality is differentially related to adiposity in adults. Psychoneuroendocrinology 98, 46–51. [PubMed: 30098512]

Tabak AG, Herder C, Rathmann W, Brunner EJ, Kivimaki M, 2012 Prediabetes: a high-risk state for diabetes development. Lancet (London, England) 379, 2279–2290.

Taheri S2006 The link between short sleep duration and obesity: we should recommend more sleep to prevent obesity.Arch Dis Child 91:881–884. [PubMed: 17056861]

Weyer C, Bogardus C, Pratley RE, 1999 Metabolic factors contributing to increased resting metabolic rate and decreased insulin-induced thermogenesis during the development of type 2 diabetes. Diabetes 48, 1607–1614. [PubMed: 10426380]

Yadav D, Cho KH, 2018 Total Sleep Duration and Risk of Type 2 Diabetes: Evidence-Based On Clinical and Epidemiological Studies. Current drug metabolism 19, 979–985. [PubMed: 29956620]

Zhu B, Hershberger PE, Kapella MC, Fritschi C, 2017 The relationship between sleep disturbance and glycaemic control in adults with type 2 diabetes: An integrative review. Journal of clinical nursing 26, 4053–4064. [PubMed: 28544107]

Highlights

- Poor sleep quality was related to glucose intolerance in people with prediabetes.
- C-reactive protein was greater in subjects with prediabetes compared to those with normal glucose tolerance.
- There was a positive correlation between sleep disturbance and C-reactive protein levels in subjects with prediabetes.

Table 1.

Characteristics of study participants in the normal glucose and prediabetes groups

Variables	NGT	prediabetes	*p* values
N (participants)	95	60	
Age, years	36.0±1.2	41.0±1.7	0.02
Gender, Female/Male, n	66/29	28/32	0.001
Race, CC/AA, n	39/56	35/25	0.08
Education levels, ≥12 years, n (%)	77 (81%)	45 (75%)	0.36
Employment status, yes/no, n	64/31	36/24	0.18
Body mass index, kg/m^2	29.2±0.7	30.6±1.0	0.24
Systolic blood pressure (mmHg)	119.4±2.0	119.4±1.9	0.98
Diastolic blood pressure (mmHg)	74.3±1.1	76.4±1.3	0.23
Fasting plasma glucose, mg/dl	91.6±0.6	105.0±0.9	0.000
2-h plasma glucose, mg/dl	93.9±1.9	118.5±3.9	0.000
BDI score	10.9±1.6	10.7±1.6	0.94

Note: NGT: normal glucose tolerance; CC, Caucasians; AA, African Americans; BDI, Beck Depression inventory

Table 2.

Comparisons of sleep quality in the normal glucose and prediabetes groups

Variables	NGT	prediabetes	*p* values
Global PSQI score	5.97±0.4	7.17±0.7	0.13
PSQI≥5, %	46	62	0.06
Sleep quality	0.88±0.08	1.07±0.13	0.19
Sleep latency	0.98±0.11	1.17±0.15	0.32
Sleep duration	0.86±0.10	0.95±0.13	0.59
Sleep efficiency	0.57±0.10	0.79±0.15	0.22
Sleep disturbance	1.24±0.08	1.39±0.09	0.24
Use of sleep medication	0.49±0.11	0.77±0.16	0.13
Day dysfunction	0.87±0.10	1.09±0.13	0.18

Note: NGT: normal glucose tolerance; PSQI, Pittsburgh Sleep Quality Index.

Table 3.

Correlations between sleep measures and glucose parameters adjusted with gender, age and BMI in participants with prediabetes

	Global PSQI	Sleep quality	Sleep latency	Sleep duration	Sleep efficiency	Sleep disturbance	Use of sleep meds	Daytime dysfunction
Fasting Glucose	0.21	0.23	0.20	0.10	0.14	0.24	0.03	0.14
0.5-h Glucose	−0.12	0.05	−0.18	−0.15	−0.13	−0.09	0.00	−0.09
1-h Glucose	−0.01	0.05	−0.03	−0.10	0.02	−0.01	0.05	−0.04
2-h Glucose	0.02	−0.06	0.05	−0.05	0.04	0.25	0.04	−0.10
AUC Glucose	0.18	0.19	0.15	−0.06	0.20	0.18	0.12	0.17

Note: Meds, medications; h, hour; BMI, body mass index; AUC, area under curve. N=60 participants in prediabetes group.

Table 4.

Comparisons for inflammatory factor in the normal glucose and prediabetes groups.

Inflammatory Factors	Normal glucose group	Prediabetes group	*p* values
Log_{10}CRP	0.18±0.06	0.37±0.07	0.03
Log_{10}IL-6	−0.16±0.03	−0.11±0.04	0.26
Log_{10}IL-8	0.83±0.06	0.91±0.03	0.07
Log_{10}IL-10	−0.40±0.05	−0.49±0.06	0.28
Log_{10}TNFa	0.39±0.02	0.38±0.02	0.88

Note: Data are presented in their log-transformed values. CRP, C-reactive protein; IL, interleukin; TNFa, tumor necrosis factor alpha.

Table 5.

Correlations between sleep measures and inflammatory factors adjusted with gender, age, and BMI in participants with prediabetes

	Global PSQI	Sleep quality	Sleep latency	Sleep duration	Sleep efficiency	Sleep disturbance	Use of sleep meds	Daytime dysfunction
Log_{10}CRP	.19	.06	.21	.06	.17	.30*	.11	.14
Log_{10}IL-6	.07	.11	.06	−.01	.08	.05	.13	−.10
Log_{10}IL-8	.08	.06	.14	−.08	.07	.15	.23	−.17
Log_{10}IL-10	−.04	−.05	−.04	−.17	.09	−.12	.12	−.12
Log_{10}TNFa	.12	−.03	.13	.05	.21	.09	.20	−.04

Note:

*$p<0.05$

PSQI, Pittsburg Sleep Quality Index; Meds, medications; BMI, body mass index; CRP, C-reactive protein; IL, interleukin; TNFa, tumor necrosis factor alpha. N=60 participants in prediabetes group.