Effects of three weeks of mild sleep restriction implemented in the home
environment on multiple metabolic and endocrine markers in healthy young
men

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Abstract

Objectives; Evidence for a causal relationship between sleep-loss and metabolism is derived primarily from short-term sleep deprivation studies in the laboratory. The objective of this study was to investigate whether small changes in sleep duration over a three week period while participants are living in their normal environment lead to changes in insulin sensitivity and other metabolic parameters.

Methods; Nineteen healthy, young, normal-weight men were randomised to either sleep restriction (habitual bedtime minus 1.5 hours) or a control condition (habitual bedtime) for three weeks. Weekly assessments of insulin sensitivity by hyperinsulinaemic-euglycaemic clamp, anthropometry, vascular function, leptin and adiponectin were made. Sleep was assessed continuously using actigraphy and diaries.

Results; Assessment of sleep by actigraphy confirmed that the intervention reduced daily sleep duration by $01:19 \pm 00:15$ (SE; $p < 0.001$). Sleep restriction led to changes in insulin sensitivity, body weight and plasma concentrations of leptin which varied during the three week period. There was no effect on plasma adiponectin or vascular function.

Conclusions; Even minor reductions in sleep duration lead to changes in insulin sensitivity, body weight and other metabolic parameters which vary during the the exposure period. Larger and longer longitudinal studies of sleep restriction and sleep extension are warranted.

Keywords- insulin, leptin, time-course, actigraphy, adiposity

Abbreviations- Type 2 Diabetes, T2DM; pulse-wave velocity, PWV.

Introduction

Development of obesity and type 2 diabetes (T2DM) in humans is multifactorial and there is accumulating evidence from epidemiological studies that besides the traditional risk factors such as excessive fat intake and a sedentary lifestyle, novel risk factors, such as short-sleep duration [1, 2] and disruption of circadian rhythms [3] should be considered. Investigating sleep duration as a risk factor is also supported by recent findings in basic circadian rhythm research which have underscored the interrelatedness of sleep-wake cycles, circadian rhythmicity and metabolism [4, 5].

The current evidence that sleep duration is a causal factor in the development of obesity and/or T2DM is limited. Although prospective cohort studies have repeatedly linked short-sleep to a variety of cardiometabolic risk factors, such as increased body weight, glucose intolerance and high blood pressure (reviewed in [6, 7]) neither causality nor the direction of the causality can be derived from these studies [8]. Furthermore, cohort studies typically rely upon subjective responses to a single sleep question, which usually does not distinguish between “sleep duration” and “time in bed”; two measures which may not always have a linear relationship to each other [9].

Laboratory studies in which sleep duration has been reduced under controlled conditions have provided evidence that acute sleep restriction leads to changes in appetite regulating hormones such as leptin and changes in insulin sensitivity and other metabolic parameters. Although these acute studies provide a potential mechanism whereby sleep duration and obesity may be linked, the relevance of these findings has been questioned. The sleep restriction in most laboratory studies has been extreme (0 to 4 hours of sleep duration) [10, 11] -[12] often compared to a longer than normal sleep duration (10 hours)

[13] and only imposed for a short period (1 to 14 days) [13]. Therefore the findings of these protocols may not be transferrable to the link between sleep and obesity in society.

The lack of adequate interventional data has been highlighted repeatedly [14-16] and in this study we conducted a controlled trial in healthy lean individuals using a moderate level of

5 sleep-loss (1.5 h per night) over a period of 3 weeks while participants were living in their normal environment, using a similar sleep protocol to that previously described by Zielinski and colleagues in older long-sleepers [17, 18]. We also used a parallel group design in which the sleep restriction was compared to a control group with no change in sleep duration, rather than a cross-over design in which the effects of sleep restriction are compared to a period of
10 recovery sleep-extension or recovery [19]. The aims in this study were, (i) To assess whether sleep duration assessed using sleep diaries and actigraphy - a reliable and validated measure of sleep duration [20], could be manipulated adequately at home rather than in a controlled sleep-laboratory environment in healthy young men, (ii) to assess whether a smaller amount of sleep loss (1.5 hours), over a period of three weeks, has an impact on insulin sensitivity
15 as assessed through hyperinsulinaemic-euglycaemic clamp, the gold-standard approach and (iii) to assess the time-course of the changes in sleep and metabolic parameters over the three week period.

Methods

Healthy male students, aged 20-30 years, BMI 19-26 kg/m² were recruited for this randomized-controlled sleep intervention study through advertisements and posters.

Initially subjects were required to complete medical and sleep questionnaires. Only those
5 with a self-reported sleep length of 7.0 -7.5 h were invited for more detailed screening. The absence of T2DM or other metabolic disease was determined by a fasting blood sample for the assessment of glucose, insulin, haemoglobin and a full blood count as well as information from the self-reported medical questionnaires. According to self-report, volunteers were not taking prescription or over the counter medication and had a stable weight for > 3 months.

10 Specific exclusion criteria also included (i) shift-work and travel beyond 2 time zones in the preceding 2 months, (ii) high intake of caffeine and alcohol, (iii) extreme morning or evening preference assessed with the Munich Chronotype and Horne Östberg Questionnaire, (iv) a self-reported sleep problem (Pittsburgh Sleep Quality Index global score ≥ 6) and (v) daytime naps in the preceding 4 weeks. The protocol was approved by the Surrey Research and the
15 University of Surrey Ethical Committees. Written informed consent was obtained from all participants.

Habitual sleep patterns were assessed by actigraphy and sleep diary information collected during a two week baseline period. Median time in bed during this period was determined by inspection of both the actigraphic recording for each night as well as the sleep
20 diary. Next, subjects were randomized using a web-based programme to either (i) time-in-bed minus 1.5 h per night or (ii) habitual time-in-bed. Subjects in both groups were provided with individual bed-time schedules based on their own median baseline data with individuals in the sleep restriction group required to set their alarm one and a half hours earlier than

normal. Participants were instructed not to take naps during the day. Subjects in the habitual sleep group were given their median sleep schedule and acted as a “placebo group” to control for changes in insulin sensitivity and weight that would happen naturally with time whilst on a sleep-protocol, or in response to the repeated measurements. Following a 12 hour overnight fast, participants attended the Centre for Endocrinology Diabetes and Research (CEDAR) centre following the 2-week baseline period and at weekly intervals for the 3 weeks of the intervention (Figure 1). During these visits weight, blood pressure and adiposity were measured, fasting blood samples were taken to measure leptin and adiponectin, arterial stiffness was assessed by pulse wave velocity (PWV) and 3 blood pressure measurements taken in the supine position. All anthropometric measurements and fasting blood samples were taken and a hyperinsulinaemic-euglycaemic clamp was then performed between 09:00 and 12:00 in all subjects and on each visit.

Sleep was monitored throughout the 5 week period using both actigraphy and sleep diaries. Actigraphs (AW64) are accelerometers with a sensitivity of 0.05g with a maximal sampling rate of 32Hz. Actigraphic data collected during 1.0 min epochs were analysed (high-sensitivity algorithm of the Mini Matter Actiwatch™) using Actiwatch Activity and Sleep Analysis 5 (Cambridge Nanotech, Cambridge MA). In total 700 nights of actigraphy data were analysed, only 6 nights of data were missing from the entire dataset representing a 99.1 % completion rate. No individual subject had < 6 recorded sleep nights in any 7 days period. For every nights sleep diary data were compared to actigraph data and after light out and lights on was determined the following sleep parameters were calculated: Time in bed (defined as interval between light out and lights on), sleep duration, sleep latency and fragmentation index, as calculated by Sleep Analysis 5). These parameters were calculated

for the week preceding each metabolic study and averaged to provide time-course data corresponding to the measurements taken during the study visit (hyperinsulinaemic clamp, vascular function etc) and thereby allowing correlations between the sleep data and other variables to be made.

5 Body weight and composition were measured by bioimpedance (Tanita, Arlington Heights, IL, USA), following voiding. Blood pressure was taken in the supine position after a 15 minute rest, as the mean of 3 readings. Pulse Wave Velocity as a measure of arterial stiffness in a branch of the aorta (between the carotid and femoral arteries) was measured non-invasively using Oscillometry (Vicorder system, Smart Medical Inc, La Mirada, CA).

10 **Hyperinsulinaemic-euglycaemic**

For the hyperinsulinaemic-euglycaemic clamp based on DeFronzo et al [21] adapted for a continuous insulin infusion [22, 23], two cannulae were placed in opposing arms. Blood samples were taken from an arterialised vein maintained at 35°C using a thermostatically controlled box. Following 3 fasting samples, human insulin (Actrapid, Novo Nordisk
15 Denmark) was infused continuously at a rate of 1 mU/kg/min for a period of 3 hours. Glucose concentrations were monitored at 5 minute intervals and basal levels were maintained by a variable infusion of 20 % dextrose. The mean dextrose infusion rate over the last 30 min of the clamp, after correcting for changes in plasma glucose concentration (expressed as $\text{mg glucose} \cdot \text{kg}^{-1} \cdot \text{body weight} \cdot \text{min}^{-1}$ of infusion) was determined and used as an
20 indicator of insulin sensitivity.

Blood glucose levels were measured immediately at the bedside with serum insulin measured on frozen samples. Fasting insulin sensitivity, representing primarily hepatic insulin sensitivity was also assessed by homeostatic model assessment (HOMA-IR) [24]. Plasma

glucose was measured using a Clandon Scientific analyser (Yellowsprings Inc, Yellowsprings OH, USA). Serum insulin, leptin and adiponectin were measured by radioimmunoassay using commercially available kits (Millipore, Billerica, MA), inter-assay CV < 5 %. There were no missing data points for any of the metabolic variables measured. .

5

A priori power calculation and statistics – 20 participants in this parallel trial (alpha 0.05) would yield an 80 % probability of detecting a 2.51 mg/kg/min change in insulin sensitivity (based on a treatment SD of 1.9), a 0.6 kg change in bodyweight (based on a treatment SD of 0.6) and a 0.53 ng/ml change in plasma leptin (based on a treatment SD of 0.4). All data were
10 analyzed with SAS^R version 9.1. A mixed model of variance (PROC MIXED) was applied to the data during the treatment weeks, expressed as deviation from baseline. In this model the class variables were participant, treatment and week-of-treatment and baseline values were treated as a co-variate. Participant was treated as a random effect, and week-of treatment as a repeated factor with an unstructured co-variance structure. Effects of treatment and the
15 interaction between treatment and week-of-treatment (time) were evaluated. The interaction between treatment and week-of treatment was taken as an indication of differential dynamics within the two treatment groups. Pearson correlation's coefficient was computed to assess potential relationships between sleep and metabolic variables. For these correlations change from baseline data were used and the associations were analysed for the group as a whole,
20 combining the control and sleep restricted groups with three observations per participant.

Results

There was no difference in the age or BMI of the 2 groups (Controls, n=9, 22 $\pm$ 0.9 years, 22.0 $\pm$ 1.0 kg/m²; Sleep restriction, n=10, 22.5 $\pm$ 1.0 years, 23.4 $\pm$ 0.7 kg/m²). The other baseline characteristics are summarized in Table 1. Fasting blood glucose, systolic and diastolic blood pressure were within the accepted local clinical range. Other variables such as self-reported sleep, measured sleep duration [25] and fasting leptin and adiponectin were also within the expected range for healthy people of this gender, age and degree of adiposity [26]. At baseline, time in bed as assessed by sleep diaries was 07:51 (SE 00:16) and 07:45 (SE 00:07) for the control and sleep restriction group respectively and did not differ between groups. The effect of the intervention on time in bed was significant ($p < 0.0001$) with an overall difference between the groups of 01:31 (SE 00:10) (Table 2). The intervention also affected sleep duration (assessed through actigraphy) ($p < 0.0001$) and the mean overall difference between the groups was 01:15 (SE 00:11) ($p < 0.0001$), Figure 2. In the sleep restriction group insulin sensitivity, as assessed by hyperinsulinaemic-euglycaemic clamp, initially decreased, and then recovered to baseline levels, whereas in the control group no changes were observed. In the overall analysis these dynamics were reflected in an absence of an overall effect of intervention on insulin sensitivity (NS), and some evidence for a treatment by week-of treatment interaction ($p = 0.07$). For HOMA-IR, neither a significant effect of treatment nor interaction between treatment and week-of-treatment was observed. Also, for the appetite regulating hormone leptin dynamic changes in the course of the intervention were observed. Whereas the overall effect of treatment was not significant ($p = 0.06$), the treatment by week-of-treatment interaction was significant ($p = 0.03$). Although leptin concentrations stayed near baseline in the first two weeks of restriction, they fell

sharply and significantly ($p=0.008$ week 3 vs. 2) during the third week to significantly below baseline. As such, after three weeks, leptin levels were significantly reduced following sleep restricted compared to baseline ($p=0.023$).

Whereas there was no overall effect of sleep restriction on body weight ($p=0.23$) a significant
5 interaction between treatment and week-of-treatment was observed ($p=0.003$). In the control group body weight did not change in the course of the study. In contrast, in the sleep restriction group, bodyweight fell initially below baseline (NS) and then returned to baseline as it significantly increased when comparing week 3 to week 2 (increase 0.97 ± 0.20 Kg in 7 days; $p=0.0001$).

10 No significant effects of treatment or significant interactions between treatment and the treatment by week-of-treatment interaction were observed for any of the other variables (Table 2).

The exploratory analyses of correlations between changes in both sleep and metabolic data (Table 3) reveal that over the whole study, changes in sleep duration were correlated to
15 changes in body weight ($p=0.041$). Although no difference was found in the absolute adiponectin concentration between the control and sleep restricted group, changes in adiponectin were found to be correlated to changes in insulin sensitivity measured during the hyperinsulinaemic clamp ($p=0.008$), fasting plasma glucose ($p=0.0008$) and adiposity measured by bioimpedance ($p=0.046$).

Discussion

In this study we have demonstrated the feasibility of changing sleep duration while participants live in their normal environment. The data show that under these conditions moderate levels of sleep-loss lead to changes in body weight and plasma leptin concentration, which change over time, as evidenced by significant interactions between treatment and week of exposure. Thus some of the effects of sleep restriction appear transient, i.e. we have been unable to confirm a change in insulin sensitivity beyond one week of sleep restriction. The data clearly indicate that the effects of a reduction in sleep duration may change in the course of the exposure to sleep reduction. Thus, making the extrapolation from single visit laboratory studies to epidemiological data problematic.

This sleep intervention has been performed in “the field” where participants modify their own sleep at home in a familiar environment. We deliberately did not restrict ‘activity’ or ‘diet’ as we wanted the participants to be free to make lifestyle and behavioural changes which may underlie any link between sleep deprivation, obesity and T2DM. Furthermore, it is well established that when participants record dietary intake repeatedly, this is unlikely to represent true habitual intake [27] due to conscious or sub-conscious behavioural change. The intervention was successful in reducing sleep duration by a smaller amount than in previous laboratory studies, consistent with earlier work [17] and by an amount which is relevant within the context of epidemiological studies [1, 28]. Insulin sensitivity was found affected by sleep-restriction, when measured directly using a hyperinsulinaemic-euglycaemic clamp, however, the effects appeared transient with no difference detectable after 2 or 3 weeks. The direction of this change in insulin sensitivity is consistent with those previously

observed in acute total sleep deprivation studies [29] and short duration sleep restriction studies with 4 to 5 hours of sleep [12, 13]. Very few studies investigating the effects of sleep deprivation on insulin sensitivity have used the gold-standard approach to quantify glucose uptake with the exception of Buxton et al [13], in which 5 hours of sleep per night was compared to a baseline of 10 h (5 h sleep length difference). If like Buxton and colleagues, we had truncated the study at 1 week, we too would have reported a significant impairment in insulin sensitivity (difference in IS between groups at one week; $2.55\text{mg}^{-1}.\text{kg}^{-1}.\text{min}$, $p<0.05$), extending the study to 3 weeks of sleep restriction changes the overall message considerably. In term of the mechanism regarding the transient change in insulin sensitivity, rodent studies have not shown compensatory NREMS sleep duration when sufficient amounts of sleep are available for the next sleep opportunity following a period of sleep loss. However, multiple rodent studies have found adaptations or lack of NREMS SWA responses after chronic sleep restriction [30, 31] [32, 33], indeed in humans, adaptation in NREMS SWA responses has been reported to increase very little after sleep restriction [34] for four or five nights [35] . Although comparison between human and rodent studies should always be made with some trepidation, and whether the mild sleep restriction in this study would allow for some adaptation to occur, can only be determined by sleep EEG recordings

In a similar study, [36] reported the effects of a 3 h difference in bedtimes maintained over 14 days. Insulin sensitivity (measured using Intra Venous Glucose Tolerance Test; IVGTT) was significantly decreased by 17.5 %. We were unable to find such an impact on insulin sensitivity when bedtime was reduced by only 1.5h.

The observation that sleep restriction affects leptin is in accordance with epidemiological data showing short sleep duration associates with reduced leptin [37]. In

laboratory studies sleep restriction has been reported to lead to both a decrease [38] or increase [10, 39] depending on study design. The inconsistent effects of sleep on leptin as reported in the literature may be related to variation in study population and gender in particular, duration of sleep restriction and severity of sleep restriction. However, there
5 appears no consistency in whether the period of sleep loss (either in hours lost per night, or duration of intervention) is related directed to the plasma leptin levels reported. Interestingly in the present study, reduction of leptin was observed only in the third week of sleep reduction and coincided with an increase in bodyweight, which initially appears counter-intuitive but corresponds well to what is found in cohort studies (reviewed by [40]). Leptin
10 expression may be inhibited directly by catecholamines [41] . The effects of lowered levels of leptin on hypothalamic centres regulating appetite, would potentially lead to increased food intake and weight gain. Changes in leptin may also be linked to changes in sympathovagal balance [19] which in turn may lead to an increase in insulin resistance within adipose tissue and an increase in lipolysis [42]. Currently there are no data linking adipocyte
15 function *in vivo* in humans directly to sleep-restriction.

The present data highlight the need to study the dynamics of the effects of sleep restriction on leptin, and these changes which occur with time may explain some of the discrepancies in the literature. To our knowledge, as this is the first time-course study investigating sleep-loss and so also the first interventional study to document effects of sleep
20 restriction on body weight, in a direction consistent with both epidemiological data and data on sleep duration and diet-induced weight-loss [43]. Clearly longer-term studies in the area of sleep duration and energy balance with the appropriate measurement of both energy intake and expenditure are now warranted. It is likely, based on the literature and the decrease in

leptin predisposing to increased food intake, that changes in energy balance would due to either increased eating opportunity or indeed increased preference for energy dense foods [19] and snacking [44, 45], although this remains to be tested fully.

Overall our data show that minor (1.5 h) changes in bedtime lead to dynamic changes in multiple variables related to metabolism in young adults, consistent with both epidemiological and laboratory studies. The correlations between the changes of many of these variables appeared meaningful within the context of our current knowledge about the inter-related network of physiological changes related to sleep loss. The original work by [17] found no effect of a 90 min reduction in sleep duration in older longer-sleepers over a period of 8 weeks assessed using an oral glucose tolerance test (OGTT) which has been confirmed here, however, more recently it was reported [25] that in healthy *young* men and women with a family history of T2DM, a 1.5h habitual curtailment in sleep-length was associated with insulin resistance and hypinsulinaemia but normal glucose tolerance. The reason for the discrepancy isn't clear but may relate to the age and habitual sleep patterns of the subject groups (ie. young v's old; long-sleepers v's short sleepers)

Strengths and Weaknesses. Our study design and interpretation of the data has a number of limitations. The sample size is small, the age range of the subjects is limited and the BMI of these subjects is within a normal range, making extrapolation to the wider population difficult. We did not obtain measures of appetite, food intake or energy expenditure although this was intentional. A strength is that the study investigated whether sleep could be controlled in the "field" and whether minor "ecologically relevant" changes in sleep could have an impact on metabolism. It is clear that we still do not fully understand the time effects in the metabolic response to sleep restriction and that some aspects of human

physiology may be adaptive in this respect, and some may not. Future interventional studies of sleep duration and metabolism over longer periods while participants are living in their normal environment are warranted. If these studies yield positive results the findings could be translated into lifestyle ‘sleep’ advice for obese people and patients [46].

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MDR conducted the clinical experiments, analysed the data and wrote the manuscript, DR-J supervised the clinical work, AMU was involved in funding and supervision and D-JD analysed the data and wrote the manuscript.

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Figure Legends

Figure 1. Protocol design. After a period of 2 weeks sleep monitoring at home (actigraphy and daily sleep diary), clinical measurements including weight, % body fat, blood pressure and insulin sensitivity by hyperinsulinaemic-euglycaemic clamp were performed. Nineteen participants were then randomized to either (i) continue with their habitual sleep pattern or (ii) reduce time in bed by 1.5 h/night. Clinical measurements were repeated at 1, 2 and 3 weeks.

- 10 Figure 2. Changes from baseline for sleep duration, insulin sensitivity (hyperinsulinaemic-euglycaemic clamp), plasma leptin, and body weight in the control group (open circles) and sleep restriction group (closed circles). Values represent the LSMEANS estimates and their standard error. N=9 for the control group and N=10 for the sleep restriction group. T (effect of treatment); T*W (Interaction of Treatment and Week-of-Treatment). #p<=0.05'
- 15 ##P<=0.01; ###; p<=0.001. Contrasts are between Treatments.

Table 1 Baseline sleep and metabolic variables in a group of 19 healthy young men following randomization to either habitual sleep or restricted sleep groups (habitual – 1.5h sleep per night). Data are presented as mean (SD). There was no significant difference between the groups at baseline.

	Habitual Sleep (n=9)	Restricted Sleep (n=10)
Self-reported Sleep ^a (hh.mm)	07:51 (00:51)	07:45 (00:24)
Measured sleep duration ^a (hh.mm)	06:05 (00:48)	06:14 (00:33)
Sleep Latency ^a (hh:mm)	00:20 (00:09)	00:22 (00:08)
Fragmentation Index ^a (%)	33.3 (9.38)	30.67 (7.43)
Adiposity ^b (%)	13.2 (5.3)	16.1 (5.5)
Body Weight (kg)	71.4 (10.67)	75.9 (7.46)
Systolic BP (mmHg)	121 (11)	119 (8)
Diastolic BP (mmHg)	68 (8)	68 (7)
Pulse Wave Velocity ^c (m/s)	6.7 (0.7)	6.8 (0.7)
Fasting Glucose (mmol/l)	4.2 (0.4)	4.2 (0.3)
Insulin sensitivity ^d (mg glucose.kg ⁻¹ .min ⁻¹)	10.33 (3.14)	10.13 (2.12)
HOMA-IR	1.9 (0.5)	1.8 (0.5)
Fasting Adiponectin (ng/ml)	6592 (2478)	8545 (2954)
Fasting leptin (pmol/l)	2.3 (1.3)	4.8 (1.6)

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a. Calculated from a combination of sleep diary and actigraphy during 2 week baseline period.

b. Assessed with bioimpedance (Tanita, Arlington Heights, IL, USA)

1. Assessed using pulse wave velocity (PWV) between carotid and femoral artery sites.

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2. Derived from the hyperinsulinaemic-euglycaemic clamp

Table 2. Change from baseline values (LSmeans) of sleep and metabolic parameters during a 3 week longitudinal study in both the habitual sleep group and the sleep restricted group (habitual – 1.5 sleep/night). Data are presented as Mean (SE of the response)

	Week 1		Week 2		Week 3	
	Habitual	Restricted	Habitual	Restricted	Habitual	Restricted
Time in Bed (hh:mm)	-00:09 (00:12)	-01:30 (00:12)	-00:11 (00:15)	-01:13 (00:15)	00:08 (00:12)	-01:26 (00:11)
Sleep latency (hh:mm)	-00:04 (00:02)	-00:08 (00:03)	00:00 (00:03)	-00:08 (00:03)	-00:05 (00:03)	-00:04 (00:03)
Fragmentation Index (%)	-1.45 (1.50)	-0.26 (1.64)	-2.32 (2.39)	0.40 (1.98)	0.01 (1.47)	0.61 (1.85)
Adiposity (%)	0.09 (0.46)	-0.82 (0.44)	0.08 (0.65)	-0.81 (0.61)	0.02 (0.6)	-0.49 (0.57)
HOMA-IR	-0.28 (0.07)	0.09 (0.07)	-0.13 (0.15)	-0.08 (0.14)	-0.15 (0.12)	-0.04 (0.12)
Fasting glucose (mmol/l)	-0.06 (0.13)	-0.04 (0.12)	-0.1 (0.11)	0.05 (0.1)	0.00 (0.11)	0.09 (0.1)
Fasting Adiponectin (ng/ml)	-165 (334)	-397 (393)	-402 (487)	-349 (461)	-702 (495)	-1016 (469)
PWV (m/s)	-0.1 (0.23)	0.04 (0.22)	0.11 (0.17)	0.28 (0.17)	0.01 (0.19)	-0.34 (0.18)
Systolic BP (mmHg)	1.0 (3)	-1 (3)	0.00 (2)	-4 (2)	-5 (2)	-3 (2)
Diastolic BP (mmHg)	0.00 (2)	-3 (2)	-2 (2)	-4 (2)	-4 (2)	-5 (2)

- 5 Metabolic and sleep variables did not differ significantly with the exception of time in bed ($p < 0.001$).

Table 3. Correlations between **change** in sleep parameters and metabolic variables. Pearson correlations were computed on data expressed as change from baseline, during the 3 weeks of the intervention for the control and interventional group **combined** (19 participants, 3 observations per participant; n = 57 observations. Values represent the correlation coefficient (rho) and the associated p value. *P ≤ 0.05 was used for significance.

	Δ sleep duration	Δ body weight	Δ % body fat	Δ Insulin sensitivity	Δ HOMA	Δ fasting glucose	Δ fasting leptin	Δ fasting adiponectin
Δ sleep duration	1.000	0.271* <i>0.041</i>	0.182 0.174	0.188 0.160	-0.071 0.599	-0.122 0.365	0.030 0.820	0.094 0.487
Δ body weight		1.000	0.251 0.058	-0.209 0.118	-0.058 0.665	-0.231 0.082	-0.197 0.139	0.234 0.079
Δ % body fat			1.000	-0.037 0.780	-0.142 0.291	-0.292* <i>0.027</i>	0.080 0.551	0.265* <i>0.046</i>
Δ Insulin sensitivity				1.000	0.001 0.992	0.381* <i>0.003</i>	-0.228 0.087	-0.344* <i>0.008</i>
Δ HOMA-IR					1.000	0.350* <i>0.007</i>	0.012 0.924	-0.223 0.094
Δ fasting glucose						1.000	0.211 0.113	-0.432 <i>0.0008</i>
Δ fasting leptin							1.000	0.185 0.166