Master's thesis

NTNU
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Potential association between chronic sleep deprivation and energy metabolism in individuals with obesity

Master's thesis in Clinical health science, obesity and health
Supervisor: Catia Martins

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Anne Mette Munch-Thore

Abbreviations

BMI - Body mass index

FatOx – fat oxidation

FFM - Fat Free mass

FM - Fat mass

EE – Energy expenditure

EI – Energy intake

EIEE – Exercise-induced energy expenditure

Net EIEE - Net exercise-induced energy expenditure

NEAT - Non-exercise activity thermogenesis

IC - Indirect calorimetry

MET - metabolic equivalent of task

OB – Obese

RCT - Randomised controlled trials

RMR – Resting metabolic rate

RQ - respiratory quotient

TEE – Total energy expenditure

PSQI – Pittsburgh sleep quality index

PA – Physical activity

PSG - Polysomnography

Abstract

Introduction: The majority of evidence from clinical studies shows that acute sleep deprivation is not associated with decreased energy expenditure (EE). However, the influence of chronic sleep deprivation on EE has not been properly investigated. Therefore, the aim of this study was to assess if chronic sleep deprivation/quality was associated with energy expenditure variables in individuals with obesity.

Method: This was an observational (cross-sectional) study in a population of 100 individuals (55 females) with obesity (BMI: 36.6 ± 4.2 kg/m^2) and median age 42.6 (± 9.7 years). Sleep duration and quality was measured with Pittsburgh Sleep Quality Index (PSQI). Sleep duration and physical activity was also measured objectively using SenseWear armbands. Resting metabolic rate (RMR), respiratory quotient (RQ) and exercise induced energy expenditure (EIEE) were assessed using indirect calorimetry. EIEE was measured on a graded cycle ergometer, were participants pedalled at 60 rotations per minute against graded resistance. Multiple regression analysis was used, using metabolic variables as dependent variables and sleep variables as predictors, after adjusting for potential confounders.

Results: Sleep duration was 6.7 ± 1. 0 h/night and 6.5 (6, 7.2) hours/night from PSQI and arm bands, respectively, and the mean sleep quality form the global score was 5.5 (±2.6). The majority of the participants reported a poor overall sleep quality (66%) and almost 70 % of the participants experienced daytime dysfunction more than once a week. No significant associations were found between habitual sleep duration, assessed through the PSQI or armbands, or overall quality from the PSQI, and any energy expenditure variable assessed. The only exception was for Net EIEE 25W, where a positive significant association (B Coeff = 0.26, P=0.03) was found between Net EIEE 25 W and sleep duration from the armbands.

Conclusion: No association seems to exist between habitual sleep quality or duration and RMR or fat oxidation (FatOx). A positive association between habitual sleep and EIEE seem to exist but more studies are need to confirm this finding.

Sammendrag

Hensikt: Konklusjonene fra flertallet av tidligere kliniske studier viser at akutt søvnmangel ikke er assosiert med redusert energiforbruk. Det finnes imidlertid lite forskning på hvordan kronisk søvnmangel påvirker energiforbruket. Målet med denne studien var derfor å vurdere om kronisk søvnmangel og søvnkvalitet var assosiert med energiforbruk hos individer med fedme.

Metode: Dette var et prospektiv kohortstudie studie med 100 deltakere (55 kvinner) med fedme (BMI: 36.6 ± 4.2 kg/m^2) og gjennomsnittlig alder på 42.6 (± 9.7) år. Søvnvarighet og kvalitet ble rapportert ved hjelp av Pittsburgh Sleep Quality Index (PSQI). Søvnlengde og fysisk aktivitet ble objektiv målt ved bruk av SenseWear armbånd. Hvileforbrenning (RMR), respirasjonskvotient (RQ) og energiforbruk under fysisk aktivitet (EIEE) ble målt ved hjelp av indirekte kalorimetri. Deltagerne sin EIEE ble målt under aktivitet på en ergometersykkel, med 60 omdreininger per minutt med gradert motstand. Etter justering for potensielle forstyrrende (konfunderende) variabler ble multiple regresjonsanalyser benyttet, der metabolske parameter ble brukt som utfallsvariabler og søvnvariabler ble brukt som prediktorer.

Resultater: Søvnvarighet ble målt til 6.7 ± 1. 0 timer/natt fra PSQI og 6.5 (6, 7.2) timer/natt fra SenseWear armbånd. Gjennomsnitt søvnkvalitet fra PSQI hadde totalskåre 5.5 (±2.6). Flesteparten av deltagerne rapporterte dårlig søvnkvalitet (66%) og opplevde nedsatt dagtid funksjon mer enn en gang pr uke (70%). Ingen signifikant assosiasjon ble funnet mellom søvnvarighet eller søvnkvalitet, målt ved bruk av PSQI eller armbånd og undersøkte metabolske variabler. Eneste unntak var Net EIEE 25W, hvor det ble funnet en positive signifikant assosiasjon (B Coeff = 0.26, P=0.03) mellom Net EIEE 25 W og søvnvarighet fra armbåndene.

Konklusjon: Ingen assosiasjon ble funnet mellom søvnvarighet eller søvnkvalitet og RMR eller RQ (fettoksidasjon). Det finnes muligens en positiv assosiasjon mellom søvnvaner og EiEE, men flere studier er påkrevd for å kunne bekrefte dette.

Relevance

Several studies have identified sleep deprivation as a potential risk factor for long-term weight gain and obesity. Although increased energy intake due to sleep loss has been listed as the main mechanism, one should also consider possible effect on energy metabolism to understand better the potential impact of sleep deprivation on the regulation of energy balance. However, the relative role of each determinant that could potentially link chronic sleep deprivation to obesity remains controversial.

A better understanding of this is important as it has implications for obesity management and prevention. This study showed that chronic sleep deprivation is not associated with changes in energy metabolism, suggesting that the association between sleep deprivation and weight gain/obesity is mainly mediated by increased appetite. However, more studies are needed to confirm these findings.

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1.0 Background

1.1. Introduction

Sleep is an essential component of healthy development and is required for physical and mental health in humans (1). Despite strong evidence indicating the importance of sleep, insufficient levels has become widespread. In children and adolescents, international findings show that sleep length (from 10-15 year) has been reduced by 23-44 minutes in the period 1985 to 2004 (2, 3). Studies among adults in Norway have found that the incidence of insomnia has increased from 11,9 % to 15,5 % in the period 2001 to 2011 and that approximately 13.6% are dissatisfied with their sleep habits (4). Furthermore, around 30 % of adults in United States report sleeping less than 6 hours per night (5-7).

The reason for the decrease in sleep is uncertain, but it may be linked to increased usage of electricity and light, technology and modern lifestyle (5, 8-10). Specifically, sleep deprivation is thought to be due to increased screen time, like television viewing, computer games, and use of Internet and mobile phones (4, 9, 11). Chronic short and poor sleep quality may lead to several negative health consequences, such as overweight and obesity, fatigue, heart disease, hypertension, depression, impaired immune functions, type 2 diabetes, etc. (12-16). In recent years, several epidemiological studies have demonstrated a correlation between sleep deprivation and increased risk of obesity (15, 17-22). Furthermore, numerous longitudinal studies have found sleep deprivation to be associated with weight gain (17, 23-29).

The trend toward decreased sleep duration and reduced sleep quality has been paralleled by an increase in prevalence of obesity which has nearly tripled between 1975 and 2016, and has become a epidemic worldwide (30). Global estimates from WHO show that in 2016, 39 % of adults were overweight and 13 % were obese (OB) (30). In the US, each year obesity-related conditions cost over 150 billion dollars and cause an estimated 300 000 premature deaths (31). Obesity is defined a serious, chronic disease (31) that can have a negative effect on many systems in your body and increases the risk for developing multiple disease conditions, such as cardiovascular disease, cancer, hyperlipidaemia, hypertension, osteoarthritis, depression and type 2 diabetes (32-34), all of which have negative effects on life quality, work productivity, and healthcare costs. When daily energy intake (EI) exceed energy

expenditure (EE), the energy balance in the body becomes positive and can lead, if sustained, to long-term weight gain and alterations in metabolic pathways (34). How insufficient sleep contributes to this risk of weight gain and obesity is unclear, as studies investigating effects of sleep deprivation on energy balance components report conflicting findings (9).

Studies have found that sleep affects energy metabolism (6). However, the effects of sleep restriction on energy metabolism and appetite remain controversial and it also remains unclear whether the association between obesity and sleep disturbances arises from increased EI alone, or a combination of increased EI and reduced EE (12, 35, 36). The impact of sleep deprivation on EI is likely to be multifactorial, and numerous mechanisms have been proposed and examined (37). Sleep has a major role in modulating hormonal release, glucose regulation and cardiovascular function and the increased risk for obesity is possibly linked to the effect of sleep loss on hormones that play a major role in the central control of appetite and EE (7, 18, 24). Several studies have found an association between sleep deprivation and deregulated appetite control due to change in the secretion of leptin (suppresses appetite) and ghrelin (stimulates appetite) (15, 23-25). Emerging hedonic pathways provide an additional potential mechanism by which sleep loss could lead to changes in dietary intake and eating behaviour (38, 39). Furthermore, short sleepers have more awakening hours, which present opportunities to increase food intake, with increased preference for carbohydrate-rich and energy-dense foods and snacks (40-42). Results from clinical studies vary, but the majority of the evidence shows that acute sleep deprivation is associated with increased EI (37, 43). Yet, it still remains unclear whether decreased EE, that is an important contributor to energy balance and weight management, also plays a role.

Insufficient sleep can have a positive or a negative effect on all components of total energy expenditure (TEE) (44), either as a consequence of increased time awake, a disturbed metabolism and/or as behavioural changes. The effects of sleep deprivation on EE are controversial and it has been theorized that a central physiological role of sleep is the conservation of energy and that the energy costs associated with sleep restriction may lead to a compensatory decline in next-day resting metabolic rate (RMR)(45). RMR is the largest (60-70 %) component of EE and the hypothesis is that a low relative RMR is associated with body weight gain in the long run (46-48). Several laboratory studies, but not all (46, 49-51) support this compensatory hypothesis and have reported decreased RMR after acute sleep restriction (45, 52-54). Furthermore, it has been theorized that sleep deprivation increase

respiratory quotient (RQ) (55, 56). RQ is an index of substrate utilization, and higher values indicate preference for carbohydrate vs. fax oxidation (56). Substrate utilization, the type of fuel used for energy, can be assessed using respiratory quotient (RQ; CO2 produced/O2 consumed). RQ ranges from 0.7 (fat metabolism) to 1.0 (carbohydrate metabolism) with higher RQ values associated with overfeeding and weight gain (47, 57, 58). The hypothesis is that subjects with a lower fat oxidation rate (FATOX) gain weight because they are more likely to store excess energy as adipose tissue. Some studies have found that acute sleep loss increase RQ (51, 53, 59), others have found it has no effect (46, 49). In addition, it is presumed that insufficient sleep may lead to increased tiredness, which is likely to affect physical activity (PA), through both a reduction in non-exercise activity thermogenesis (NEAT) and planned PA (60).

Despite the suggestion of a reduction in RMR as a physiological adaptation to insufficient sleep, many sleep deprivation studies have demonstrated that restricting sleep duration does not alter RMR (37, 40, 50, 61, 62). This may be a result of the fact that most studies are acute laboratory-controlled studies with restricted duration (normally 1-5 nights), have a small sample size and vary regarding age, sex distribution and body mass index (BMI) (60). The majority of the studies were also done in healthy normal-weight males, which may contribute to inconsistent findings, therefore the conclusions cannot be generalized to the entire population. However, a couple of studies with a longer duration (2-3 weeks long) show reduced RMR and increased RQ after sleep deprivation (53, 54). A 14 day clinical laboratory sleep restriction study in 10 overweight adults (70% males) following a hypocaloric diet resulted in reduced EE and decreased loss of fat when sleep opportunity was restricted to 5.5 h/nigh (53). Furthermore, Buxton et al. preformed a controlled laboratory study in 21 healthy adults (10 female/11 male) with up to 3 weeks sleep restriction combined with circadian disruption, which reduced RMR significantly (-8% on average for all subjects) (54). The results of these studies could reveal adaptive or maladaptive physiological effects of sleep deprivation that would emerge beyond the immediate acute metabolic effects observed in previous shorter laboratory sleep restriction studies in humans.

To my knowledge, only one study to date has investigated the association between chronic sleep deprivation and RMR (63). De Jonge et al. reported that that poor sleep quality was associated with increased RMR and higher RQ in a cohort study of 126 individuals with obesity (BMI 38.6 +/- 6,5 kg/m2) with an average sleep duration of 6 hours +/- 50 min/night.

Small sample sizes and limited number of available studies looking at a potential association between chronic sleep deprivation and RMR and RQ makes if difficult of conclude about a potential association between these variables. Acute laboratory-controlled studies are inadequate to examine the influence of habitual sleep deprivation on EE variables. Since EE and substrate oxidation are predictors of long-term weight change, it is important to investigate the potential impact of chronic sleep deprivation on energy metabolism in a natural environment and more studies are clearly needed in this area.

1.2. Theoretical background

1.2.1 Obesity

Obesity is a result of chronic positive imbalance between EI and EE and is defined as a BMI above 30 kg/m2 (32). Worldwide, the proportion of adults with a BMI of 25 kg/m^2 or greater increased between 1980 and 2013 from 28.8 % to 36.9 % for men, and from 29.8 % to 38 % for women (33). Obesity increased from 921 million in 1980 to 2.1 billion in 2013, and was estimated to cause 3.4 million deaths globally in 2010 (33). Excessive food consumption and inadequate PA are primary factors contributing to the increase in obesity prevalence over the last decades. There are also a number of other potential contributors, including changes in the gut microbiome, changes in the composition of diet, genetics, sleep deprivation, stress, environmental, hormonal and neural factors (32).

1.2.2 Sleep

Sleep is the biologic process whereby a person leaves waking consciousness, and is characterized by changes in physiological variables like brain wave activity, breathing, heart rate, body temperature and other physiological functions (64, 65). Basal metabolic rate is reduced by 20-30 % during sleep, because less energy is needed to support brain function, sympathetic activity, breathing, circulation and core body temperature. It is regulated by neurotransmitters, that control whether we are asleep or awake by acting on different groups of neurons in the brain (66) .

The function of sleep is one of the most persistent and perplexing mysteries in biology, and many theories have been proposed to explain why we spend a third of our lives sleeping (1,

67), which includes the Inactivity theory, Energy conservation theory, Restoration theory and the Brain plasticity theory (1, 67). Although these theories remain unproven, science has made tremendous strides in discovering what happens during sleep and what mechanisms in the body control the cycles of sleep and wakefulness that help define our lives.

Sleeping can be divided into non-rapid eye movement (NREM) and rapid eye movement (REM). NREM sleep is divided into stages 1, 2, 3 and 4; from light to increasingly heavy sleep (66) and each stage is associated with distinct brain activity and changes in eye movement and muscle tone (64). Each stage is also associated with different brain waves that can be measured with electroencephalograph (EEG) (64). NREM and REM alternate in cycles each of them lasting for approximately 90-120 minutes and several rounds may occurred during one nigh of sleep (Figure 1: sleep cycles) (66).

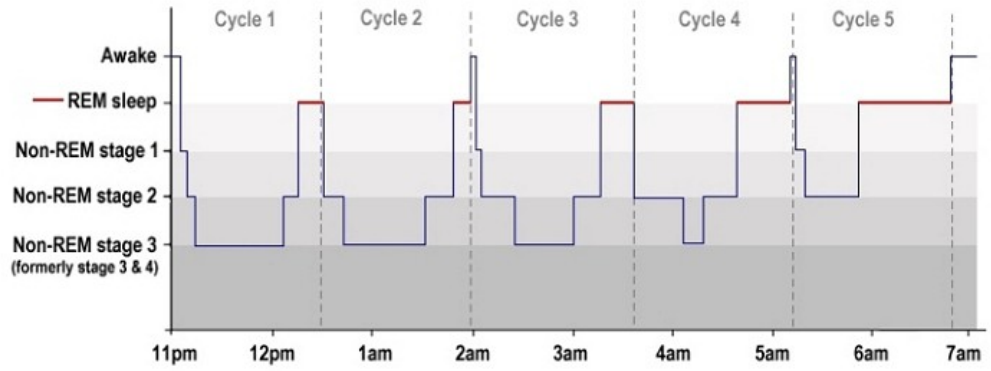


Figure 1. Sleep cycles.
A hypnogram showing sleep stages and cycles in adult sleep. Image by Luke Mastin.
Adapted from howsleepworks.com, by M. Thompson, 2019.
Retrieved from https://www.howsleepworks.com/types_cycles.html

Sleep normally begins with NREM sleep, followed by a REM sleep episode. This is called the first sleep cycle. Cycle 1 is the lightest stage of NREM sleep, and can easily be disrupted causing awakenings or arousals. In Cycle 2, our brain produces short periods of rapid, rhythmic brain waves. During this stage our body temperature drops and our heart rate begins to slow down. Cycle 3 and 4 are often referred to as slow wave sleep (SWS), which is deep, restorative sleep, that plays a significant role in declarative memory by processing and consolidating newly acquired information (1, 66). SWS mostly occurs during the first third of

the night (1). Cycle 3 and 4 is our deep sleep period, and as sleep progresses, SWS becomes increasingly shorter and REM sleep episodes are progressively longer.

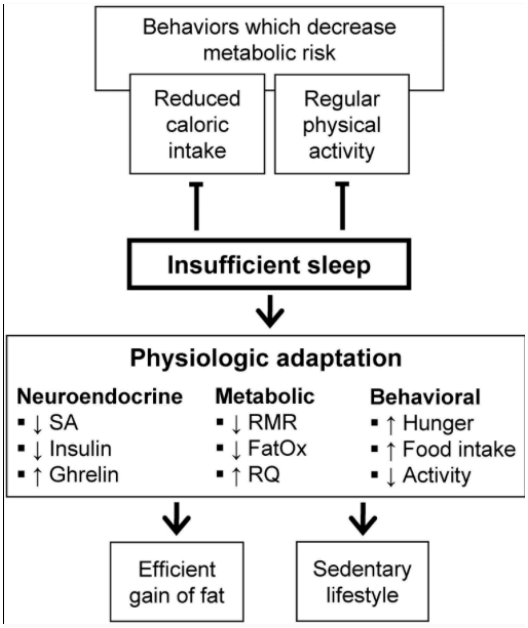
Sleep is regulated by two body systems; sleep/wake homeostasis, which monitors our need for sleep based on how long we have been awake; and the circadian biological clock, which regulates the timing of periods of sleepiness and wakefulness throughout the day (68, 69). These two systems control the sleep-wake cycle, regulate body temperature, heart rate, muscle tone, and hormone secretion, and modulate PA and food consumption (70). However, the homeostatic sleeping system can be overruled by voluntary sleep restriction and disrupted and affected by sleep-related disorders, e.g. insomnia, narcolepsy, sleep apnea (OSA) and restless leg syndrome (70, 71).

Sleep deprivation refers to the inability to obtain a sufficient amount of sleep (72). Acute sleep deprivation refers to little or no sleep, usually lasting for one day or two. In contrast, chronic sleep deprivation exists when the individual routinely sleeps less than required (72, 73). Sleep deprivation can be total (no sleep allowed), partial (either early or late sleep deprived), or selective (specific stages of sleep are deprived). Chronic sleep restriction is generally defined as habitual sleep durations of less than 7 hours, but more than 4 hours, per night (74). Lack of adequate sleep affects mood, motivation, judgment, and our perception of events and has impact on learning and memory (75). When we are sleep deprived, our focus, attention, and vigilance drifts, making it more difficult to receive information. In addition, our judgement becomes impaired. We lose our ability to make sound decisions because we can no longer accurately assess the situation, plan accordingly, and chose the correct behaviour (1).

Sleep needs vary across ages and the current National Sleep Foundation recommends to sleep between 9-11 hours for school-aged children, 8 to 10 hours for teenagers and 7-9 hours per night for adults to promote good health, and the guidelines state that under 6 hours of sleep may compromise overall health and well-being (76, 77). Chronic sleep restriction and poor sleep quality have become more common in recent decades and it is estimated that 50 to 70 million Americans chronically suffer from a disorder of sleep and wakefulness, hindering daily functioning and adversely affecting health and longevity. Sleep deprivation is increasingly recognized as a health concern, and studies have revealed that people who sleep poorly are at greater risk for a number of diseases and health problems such as hypertension, diabetes, obesity, heart attack, stroke, depression and increased mortality (1, 71). Sleep

deprivation can negatively affect a range of system in the body; it can lead to reduced immune system (reduced capasity for producing cytokines to fight infections), increased risk of respiratory diseases, weight gain by deregulating the appetite contol system and subsequently affecting the feelings of hunger and satiety, increased insulin production (increased fat storage and higher risk of type 2 diabetes), increased risk for cardiovascular diseases, altered inflammation control and dysrupted hormone production.

Several studies have linked insufficient sleep to weight gain (17, 23-29), and sleep deprivation is now seen as a potential risk factor for obesity (15, 16, 19-22), along with lack of exercise and overeating (48). Insufficient sleep triggers a set of neuroendocrine, metabolic, and behavioural adaptations aimed at increasing food intake and conserving energy (figure 2).



Figur 2. Influence of sleep deprivation on energy balance. An illustration of how insufficient sleep triggers a set of neuroendocrine, metabolic, and behavioural adaptations aimed at increasing food intake and conserving energy. *The Journal of Clinical Endocrinology & Metabolism, Volume 97, Issue 6, 1 June 2012, Pages 1792–1801, https://doi.org/10.1210/jc.2012-1067*. Copyright by The Endocrine Society

Sleep deprivation studies suggest that these changes in the regulation of energy homeostasis in response to insufficient sleep resemble the principles of human metabolic adaptation to negative energy balance (48). This metabolic adaptation, including lower anorexigenic (leptin, insulin) and higher orexigenic (ghrelin) hormone secretion aimed at increased hunger

and reduced satiety, combined with decreased sympathetic tone, lower RMR, and reduced PA to conserve energy, creates ideal conditions for weight gain (48).

1.2.3 Energy metabolism

Total energy expenditure (TEE), also known as metabolic rate can be divided into three different components; 1) resting metabolic rate under basal conditions (RMR); 2) diet-induced thermogenesis (DIT) and 3) activity-related energy expenditure (AEE) (48, 60, 78). Total daily energy expenditure can vary from person to person depending on body size, gender, body composition, genetics and activity level. RMR is the energy required to maintain essential vital functioning and is responsible for around 60-70 % of the energy-disposure during a day (79). Thermic effect of food or diet-induced thermogenesis (DIT) is the increase in EE associated with the digestion, absorption, metabolism and storage of food, and accounts for approximately 10% of TEE. AEE, the last component of TEE can be further separated into Physical activity-related energy expenditure (PAL), also named Exercise-induced energy expenditure (EiEE) and non-exercise activity thermogenesis (NEAT). AEE is the most variable component of TEE and can vary from 20-30% in sedentary populations, to over 50% for the most active individuals (60).

Each component can be measured using various methods. Total daily EE can be measured using doubly-labeled water for total free-living measurements or using a metabolic chamber, in which a person is confined to a small room while room gases are collected to assess oxygen consumption and carbon dioxide production (80). Indirect calorimetry (IC), using a ventilated hood metabolic cart, can be used to assess oxygen consumption and carbon dioxide production over several hours. With that method, the calculated EE can be extrapolated to a 24-h period. Various methods are used for gas collection, like mask, hood or canopy (81). Usually, this is the method of choice for measuring RMR, postprandial thermogenesis and EE of specific activities (80).

1.2.3.1 RMR

Resting metabolism is the energy required by your body to perform the most basic functions like breathing, circulation blood or basic brain functions, when your body is at rest after an overnight fast, and is the largest single component of total daily caloric expenditure (60). RMR is mainly determined by body size and composition (82). Although, several other

factors affect RMR; including sex, age, genetic, temperature, health, hormones and diet (83, 84).

Fat-free mass (FFM), the main determinant of RMR, accounts for 50%-70% of the variance in RMR and contains highly metabolic active tissue, such as muscle and organs, low metabolic bone and connective tissue (83). By contrast, muscle mass comprises more than 50% of FFM and account for up to 25% of RMR. Nevertheless, the amount of FFM (in kg) can vary considerably between obese and non-obese individuals and even across the spectrum of obesity itself. Overall, individuals with obesity tend to have higher absolute amounts of both fat and FFM because these variables increase concomitantly with an increase in body weight.

The metabolic rate can be measured or estimated by equations. IC is the current gold standard to measure RMR and provides the most accurate (within 5%) assessment of nutritional needs (85). Previous studies have demonstrated an association between reduced RMR and increase risk of weight gain overtime (55, 86). Furthermore, a low RMR is likely to contribute to weight regian in formerly obese persons (87).

1.2.3.2 RQ

The oxidation of the macronutrient substrates (fat, carbohydrates and protein) is an essential part of the energy balance, and changes in fat balance are highly involved in body-weight (BW) regulation, and day-to-day fluctuations. Substrate oxidation can be assessed clinically by measuring RQ, and is defined as the ratio of carbon dioxide production to oxygen consumption and reflects the relative contributions of fat, carbohydrate, and protein to the oxidation fuel mixture (47, 88). Inherent variability in substrate oxidation may be one mechanism that affects weight gain and fat storage (89).

Substrate utilization must be calculated under resting or steady-state exercise conditions (88). IC, measured with a respiratory test, allows for the assessment of RQ, and substrate utilization. IC is based on the premise that respiratory gas exchange (production of CO2 and consumption of oxygen (O2)) reflect cellular metabolic activity. RQ indicates nutrient utilization, such that a higher RQ corresponds to greater reliance on carbohydrates as the primary energy source whereas a lower RQ indicates greater fat FatOx.

The RQ typically ranges between 0.7 (fat metabolism) and 1.0 (carbohydrate metabolism), where ranges between level 0.7 to 0.85 indicates mainly fat burning, with a 100 % fat burning of 0.7. When the value reaches about 0.85, the combustion has gone on to be mainly carbohydrates, and a RQ of 1 indicates 100% carbohydrates oxidation (90). An average resting RQ of 0.82 shows that the human body derives more than half of its energy from fat (fatty-acids), and most of the rest from carbohydrate (glucose). Higher RQ values have been found to predicts fat accumulation over time (38) and are associated with overfeeding and weight gain (47, 57, 58, 88, 91). Data from previous sleep deprivation studies indicates that sleep time and sleep efficiency are important determinant of RQ (51, 53, 63). Insufficient sleep has been associated with a higher RQ, indication a shift from fat toward carbohydrate oxidation.

1.2.3.3 EiEE

Exercise induced energy expenditure (EiEE or PAL), the most variable component of TEE, can be divided into physical activity-related energy expenditure (PAL or EiEE) and non-exercise activity thermogenesis (NEAT). NEAT is EE regarding body posture and unaware movements that are associated with daily life and includes the EE of all occupation, leisure, sitting, standing, and ambulation (92). EiEE is determined by body size and body movement, and factors like intensity, duration, and frequency (48, 93). EiEE can be measured by IC for activities at a standardized speed and for the same distance, based on gas exchange measured continuously using a facemask, while activity of heart rate monitors and pedometers is used to estimate EiEE in daily life (48). EiEE can be measured in a metabolic chamber, using a metabolic cart, or by actigraphy.

Insufficient sleep can effect both EiEE and NEAT. Results from previous studies have shown a reduction in the amount and intensity of PA with sleep restriction (48, 60, 78). It is presumed that insufficient sleep may lead to increased tiredness, which is likely to affect PA, through both a reduction in non-exercise activity thermogenesis (NEAT) and planned PA (60). These results support the hypothesis that a reduction in physical activity in response to sleep loss is one of the potential causal pathways for the association of chronic sleep insufficiency with metabolic morbidity. Furthermore, sleep deprivation is hypothesized to lead to decreased energy-cost during exercise (48). However, studies of sleep deprivation and energy-cost during exercise are limited.

1.3 Aims and hypothesis

The primary aim of this study was to assess the association between chronic sleep deprivation/sleep quality and RMR in individuals with obesity. Secondary aims were to examine the association between chronic sleep deprivation/quality and FatOx and Net EIEE. The hypotheses of this master thesis was that chronic sleep deprivation (< 7 hours of sleep per night) and poor sleep quality (score <5) based on the Pittsburgh Sleep Quality Index (PSQI) global score (94) were associated with reduced RMR, decreased EiEE and higher RQ values (reduced fat oxidation) in individuals with obesity.

2.0 Method

2.1 Study design

This was an observational (cross-sectional) study, which used baseline data from a weight loss intervention trial run by the Obesity Research group at the Norwegian University of Science and Technology (NTNU) in Trondheim, Norway.

2.2 Participants

The setting took place at the Obesity centre at St. Olavs Hospital in Trondheim, Norway. Participants were recruited by newspaper advertising, announcement on the intranet of St. Olavs Hospital and NTNU and Facebook, and through flyers posted in NTNU campus Gløshaugen, and in Trondheim. In total, data from 100 healthy Caucasian participants (55 females/45 males, with BMI 36.6 ± 4.2 kg/m^2, age 42.6 ± 9.7 years) were included in this study.

2.2.1 Inclusion criteria

Healthy adults between 18 to 65 years old, both men and women, with a 30 kg/m^2 < BMI < 47 kg/m^2, weight stable (<2 kg variation in the last 3 months) and not currently dieting to lose weight were included in the study. Participants had to be sedentary and women had to be on hormonal contraceptives or be post-menopausal to take part in the study.

2.2.2 Exclusion criteria

The exclusion criteria for this study included pregnancy, breast feeding, drug or alcohol abuse within the last two years, current medication known to affect appetite or induce weight loss and enrolment in another obesity treatment program. Furthermore, history of psychological disorders, eating disorders, diabetes type 1 or 2, gastrointestinal (particular cholelithiasis), kidney, liver, lung, sleep apnea, cardiovascular disease and malignancies were additional reasons for exclusion.

2.3 Ethics

Study participation was voluntary, data was anonymized and a written informed consent was signed by the participants before entering the study (appendix 1). All data was processed confidentially and treated anonymously. The study was approved by the Regional Committees for Medical and Health Research Ethics in Midt-Norge, Trondheim, Norway (Ref.,2012/1901) and conducted according to the guidelines laid down in the Declaration of Helsinki.

2.4 Detailed protocol

2.4.1 Participation Procedure

Potential participants met for an information meeting and interview at the Obesity Research Centre for assessment of eligibility against inclusion/exclusion criteria. Those who met the criteria for inclusion in the study, were scheduled for an assessment day where a battery of tests was performed and they were given a SenseWear armband to measure PA levels prior to their test day.

2.4.2 Measurements

In the evening before the test day, participants were asked not to eat or drink anything after 8 pm except water. Participants were also asked to avoid alcohol consumption and not to perform moderate or vigorous PA 24 hours before the testing. Participants were measured in the morning after the overnight fast, and before testing had to abstain from caffeine for at least 6 hours and avoid nicotine for at least 2 hours. These guidelines were given aiming to standardize the measurement of RMR (95) and reduce the source of error.

2.4.3 Outcome variables

2.4.3.1 Body weight and body composition

BW and height were measured using standard procedures. BW was measured in fasting with an empty bladder, wearing underwear, using Seca 877 digital weight (SECA, Hamburg,

Germany). Height was measured with Seca 217 stadiometer (SECA, Hamburg, Germany) without shoes. BW was measured to the nearest 0,1 kg and height to nearest 0.5 cm.

Body composition, kilograms (kg), fat mass (FM) in percent (FM%) and FFM in percent (FFM%) were measured, using air displacement plethysmography (BodPod, COSMED, Italy) (96). Participants were fasting, with empty bladder, wearing only underwear and a swimming cap. Metal and jewellery were taken off before entering the BodPod. The body composition was calculated from the relationships between pressure and volume inside the chamber, with use of the Brozek equation and adjusted for predicted thoracic gas volume (97).

2.4.3.2 Sleep duration and quality

Subjective sleep duration and quality were measured retrospective using a Norwegian validated version of the Pittsburgh Sleep Quality Index (PSQI) (94, 98, 99). In the questionnaire, the participants were given scores on their sleep habits from 0 to 3 for each question, where 0 means no difficulty and 3 means severe difficulty. In total there are 7 component (C) scores: C1: duration of sleep, C2: sleep disturbance, C3: sleep latency, C4: day dysfunction due to sleepiness, C5: sleep efficiency, C6: overall sleep quality and C7: sleep medication, and the total PSQI global score ranges from 0 to 21, where a score > 5 indicates low sleep quality (attachment 1).

Objective sleep duration was measured by arm bands (Bodymedia, SenseWear, Pittsburgh, USA) on the back of the upper triceps of the non-dominant arm, for a 7-day period prior baseline measurement. SenseWear is a multisensory tool that uses an algorithm with data from accelerometer, heat flux and galvanic skin response, which can measure PA levels and sleep duration in a free-living environment. The arm band was originally developed as a tool for measuring PA levels, but can also be used to measure sleep duration and has been validated in a population of normal weighted individuals against polysomnography (PSG). This method is considered the gold standard for measuring sleep (100).

2.4.3.3 Metabolic components

RMR and RQ

RMR was measured in the fasting state by IC (Vmax Encore 29N, Care Fusion, Germany) using a canopy system and following standard procedures (101). While calibration of the equipment was performed, the participants rested for 10 min on a chair. After that, a ventilation hood was placed around the person's head, and O2 consumption (VO_2) and CO2 production (VCO_2) were measured for 15-20 min or until "steady state" was reached, with the participant laying in the supine position. The first 5 minutes were excluded from the calculations, and RMR and RQ were derived by taking an average of at least 5 minutes of stable data. Stable data was defined by a coefficient of variation (CV) of no more than 10 % for VO_2 and VCO_2 (101).

EiEE and RQ during exercise

EIEE was measured on a graded cycle ergometer (Monark, Eromedic 839E, GIH, Sweden). Between 2.5 and 3 hours before this test, participants were served a standardised meal with 600 kcal (17 % protein, 35 % fat, and 48 % carbohydrates). Participants pedalled at 60 rotations per minute (RPM) against graded resistance to generate 10, 25 and 50 W of power in sequential four-minute intervals. Gas exchange (VO2, VCO2 and RQ) was measured continuously using a facemask by IC (Vmax Encore 29N, CareFusion, Germany). Power generated during cycling (W) was converted into kilocalories per minute of power generated (1 W = 0.01433 kcal/min). The individual´s RMR was subtracted from the value of gross EiEE, to get the EE above RMR (net EiEE) during cycling. Data from the last 2 minutes of each stage (10, 25 or 50W) was used for the calculation of net EiEE, and to compute RQ (102).

Physical activity

To measure PA, the participants were SenseWear armband (BodyMedia, Pittsburgh, PO, USA) on their non-dominant overarm, for a period of seven days prior to their test day. SenseWear armbands have been validated to measure EE in adults (BMI: 18-35 kg/m2) (100). Data were considered valid if participants wore the armband for ≥ four days (including at least one weekday), on more than 95% (>22.8 hours/day) of the time.

The following variables were analysed: average metabolic equivalent (MET), sedentary time (<1.5 METs), and time spent on light- (1.5–<3.0 METs), moderate- (3–<6.0 METs), moderate

to vigorous (> 3 METs) and vigorous- to very vigorous activities (>6 METs), total physical activity (PA) level (>1.5 METs) and steps/day.

2.5 Power calculation

The power calculation was based on the hypothesis that RMR is significantly lower in chronic short sleepers (< 7 h pr night) compared with normal/long sleepers (> 7 h pr night). For differences in mean RMR of 0.1 kcal/min between groups and a standard deviation of 0.18 kcal/min at a power of 80% and a significance level of 0.05, 114 participants were needed in total to detect differences in RMR between the groups (45).

2.6 Statistical analysis

The statistical analysis was performed using the statistical program, SPSS version 25 (SPSS IBM, New York, USA). Statistical significance level was set at $P < 0,05$. Results are expressed as mean ± S.D, unless otherwise stated.

The Shapiro-Wilk test and Kolmogorov-Smirnov test, in addition to assessment of Q-Q plots (Quantile-Quantile) were used to check for normality for all variables. To achieve normal distribution some variables had to be transformed; weight, RMR, RQ, Net EIEE 10 and Net EIEE 25 were log transformed and for the PA variables; moderate activity, and moderate to vigorous activity were log transformed. The analysis was performed with and without outliers. Given that no differences were seen in the outcome, it was decided to keep the outliers and include all participants in the analysis. For the variable sleep quality (global score, PSQI) Q-Q plot was normal distributed after the outlier was deleted (4 SD (2.85) from the mean (5.61)). Armband sleep duration and armband average MET did not achieve normal distribution even after log transformation. Non normal distributed data are presented as median with first and third quartile.

The association between habitual sleep duration/quality and the metabolic components RMR, RQ and EiEE (Net EIEE 10, 25 and 50W) was assessed by multiple regression analysis, after adjusting for potential confounders. Metabolic variables were used as dependent variables and

sleep variables as predictors. The predictors were as follows; sleep duration from arm bands, sleep duration from PSQI, sleep quality from PSQI and component 1-7 from PSQI. Separate regression models were run for each dependent variable and for each predictor, after adjusting for age, sex and FFM for RMR, adjusting for age, sex and BMI for exercise RQ and for Net EIEE.

A linear regression model with a univariate analysis of variance was used to look for sex interaction. Sex was not a significant variable (predictor) on the metabolic components when we included gender in the regression model. Therefore, it was taken out and results are presented for all participants only.

3.0 Results

3.1 Characteristics of the subjects

One hundred participants where included in this study, and their general characteristics are presented in table 1.

Table 1: Subject characteristics

Category	Variable	Central tendency All (N=100)	Sample size[a]
General	Gender (female %)	55%	100 (55/45)
	Age (years)	42.6 ± 9.7	100 (55/45)
	Weight (kg)[b]	110.3 ± 18.4	100 (55/45)
	Height (m)	1.7 ± 0.1	100 (55/45)
	BMI (kg/m^2)[c]	36.6 ± 4.2	100 (55/45)
	FM %	44.1 ± 6.4	99 (55/44)
	FFM %	55.9 ± 6.4	99 (55/44)
Sleep	Duration (h/night), armband[d]	6.5 (6, 7.2) *	66 (40/26)
	Duration (h/night), PSQI	6.7 ± 1.0	100 (55/44)
	Quality (global score), PSQI[e]	5.5 ± 2.6	99 (55/44)
Metabolic components	RMR (kcal/day)[b]	1551 ± 305.3	100 (55/44)
	Resting RQ[bj]	0.85 ± 0.05	100 (55/44)
	Net EIEE 10 w (kcal/min)[bgh]	2.7 ± 0.7	96 (52/44)
	Net EIEE 25 w (kcal/min)[bgh]	3.4 ± 0.7	96 (52/44)
	Net EIEE 50 w (kcal/min)[bgh]	4.8 ± 0.7	95 (52/43)
Physical activity	Steps (per day)	6619.7 ± 2783.7	82 (46/36)
	Armband average MET[d]	1.2 (1, 1.3)*	82 (46/36)
	Sedentary time (min/day)	1143.4 ± 107.2	82 (46/36)
	Light activity (min/day)	213 ± 65.8	82 (46/36)
	Moderate activity (min/day)[be]	57.8 ± 38.9	80 (44/36)
	Vigorous activity (min/day)[d]	0.6 ± (0.2, 0.9)*	81 (45/36)

Data presented as mean ± SD. [a] All participants (females/males). [b]normal distributed after logarithmic transformation [c]BMI: Body-mass index (calculated as the weight in kg divided by the square of the height in meters); [d]Non-normal distributed; [e]Outlier deleted, [f]RQ: Respiratory quotient ($CO_{2eliminated}/O_{2\ consumed}$); [g]Net EIEE: Exercise induced energy expenditure (RMR subtracted from the value of gros EiEE, to get the EE above RMR during cycling) [h]W: Power generated during cycling (converted into kilocalories pr minute of power generated); *Data presented as median with first and third quartile

The participants average age was 42.6 (± 9.7) years and their average BMI was 36.6 (± 4.2) kg/m^2. There was almost an equal distribution between females and males (55 vs 45%, respectively). The mean sleep quality from the PSQI was 5.5 (±2.6) and the habitual sleep

duration derived from the PSQI was 6.7 ± 1. 0 h/night. The participants had an average of 6619.7 ± 2783.7 steps/day and average PAL was 1.2. Average moderate PA was under 1h/day (57.8 ± 38.9 (min/day)).

3.2 Overview of sleep duration and quality

Sleep duration and quality from both arm band and PSQI score are presented in table 2.

Table 2: Detailed information regarding sleep duration and quality among participants

Sleep variable	Score	All Participants N = 100
Sleep duration, arm band*	< 7 hours ≥ 7 hours	39 (59.1 %) 27 (40.9 %)
Sleep duration, PSQI	< 7 hours ≥ 7 hours	48 (48%) 52 (52%)
Global score (overall sleep quality)	0-4 = Good sleep quality 5-21 = Bad sleep quality	34 (34%) 66 (66%)
Component 1: Subjective sleep quality	0 = Very good 1 = Fairly good 2 = Fairly bad 3 = Very bad	27 (27%) 62 (62%) 11 (11%) 0 (0%)
Component 2: Sleep latency	0 = ≤ 15 minutes 1 = 16-30 minutes 2 = 31-60 minutes 3 = > 60 minutes	30 (30%) 41 (41%) 24 (24%) 5 (5%)
Component 3: Sleep duration	0 = > 7 hours 1 = 6-7 hours 2 = 5-6 hours 3 = < 5 hours	28 (28%) 39 (39%) 31 (31%) 2 (2%)
Component 4: Habitual sleep efficiency	0 = > 85% 1 = 75-84% 2 = 65-74% 3 = <65%	68 (68%) 26 (26%) 4 (4%) 2 (2%)
Component 5: Sleep disturbances	0 = 0 1 = 1-9 2 = 10-18 3 = 19-27	5 (5%) 69 (69%) 24 (24%) 2 (2%)
Component 6: Use of sleep medication	0 = Not during the past month 1 = Less than once a week 2 = 1-2 times a week 3 = Three or more times a week	90 (90%) 4 (4%) 4 (4%) 2 (2%)
Component 7: Daytime dysfunction	0 = Never 1 = Once or twice a week 2 = 1-2 times each week 3 = 3 < times each week	31 (31%) 54 (54%) 14 (14%) 1 (1%)

*** Data only available from 66 participants**

The majority of the participants reported a poor overall sleep quality (66%). Fifty-nine % and forty-eight % of the participants had short sleep duration (< 7 hours pr night) based on the arm bands and the PSQI, respectively. Almost seventy % of the participants experienced daytime dysfunction more than once a week.

3.3 Association between sleep variables and energy metabolism

Associations between habitual sleep variables and variables related to energy metabolism are presented in table 3, 4 and 5.

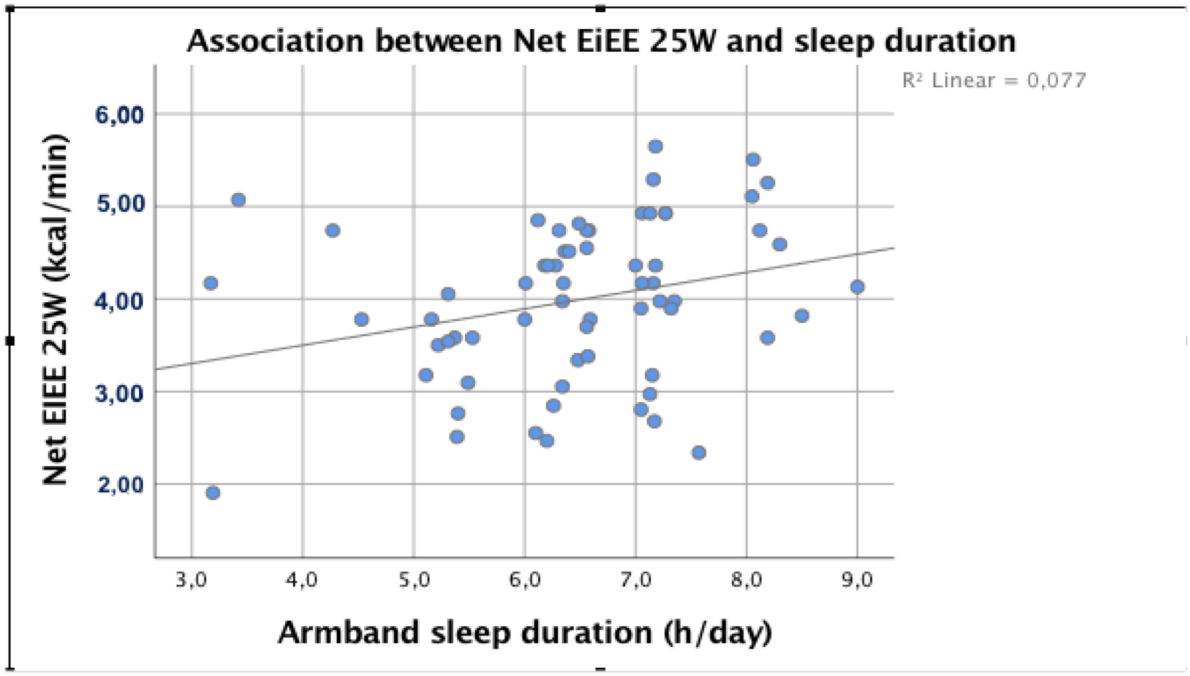
Table 3 Association between sleep variables and energy metabolism

	Sleep duration (h/day) arm bands*		Sleep duration (h/day) PSQI		Sleep quality (global score) PSQI	
	ß Coeff.	**p**	**ß Coeff.**	**P**	**ß Coeff.**	**P**
RMR (kcal/day)[ab]	-0.05	0.49	0.07	0.27	0.03	0.66
Resting RQ[ce]	0.11	0.42	0.04	0.73	-0.02	0.88
EiEE:						
Net EIEE 10 (kcal/min)[bd]	0.02	0.84	0.02	0.81	-0.06	0.54
Net EIEE 25 (kcal/min)[bd]	0.26	*0.03*	-0.16	0.12	0.01	0.91
Net EIEE 50 (kcal/min)[ed]	0.01	0.93	0.03	0.73	-0.08	0.41

Each coefficient is from a separate regression model. [a]Adjusted for age, sex, and FFM. [b]log transformed. [c]Adjusted for age, sex and BMI. [d]Adjusted for age, sex and FM. [E]outlier excluded [e]$CO_{2eliminated}/O_{2\ consumed}$ *data only available from 66 participants

No significant associations were found between habitual sleep duration, assessed either through the PSQI or armbands, or quality, derived from the PSQI, and any of the energy metabolism related variables measured. The only exception was for Net EIEE 25W, where a positive significant association (B Coeff = 0.26, P=0.03, n=66) was found between Net EIEE 25 W and sleep duration from the armbands. The scatterplot for the association between Net EIEE 25W and sleep duration from armbands can been seen in table 4.

Table 4 Association between Net EIEE 25W and sleep duration from armbands



Log transformed. Adjusted for age, sex and FM

The associations between PSQI sleep variables and energy metabolism are presented in table 5.

Table 5 Association between PSQI sleep variables and energy metabolism

	Subjective sleep quality C1, PSQI		**Sleep latency C2, PSQI**		**Duration of sleep C3, PSQI**		**Sleep efficiency C4, PSQI**		**Sleep disturbances C5, PSQI**		**Sleeping medication C6, PSQI**		**Daytime dysfunction C7, PSQI**	
	B Coeff	**P**	**B Coeff**	**P**	**B Coeff**	**P**	**B Coeff**	**P**	**B Coeff**	**P**	**B Coeff**	**P**	**B Coeff**	**P**
RMR (kcal/day)[ab]	-0.03	0.55	0.05	0.40	-0.04	0.50	0.07	0.24	0.03	0.65	0.01	0.81	0.00	0.94
Resting RQ[ce]	-0.05	0.66	0.01	0.92	-0.06	0.58	0.04	0.72	-0.02	0.87	0.03	0.81	-0.03	0.77
EIEE:														
Net EIEE 10 (kcal/min)[bd]	-0.07	0.44	-0.09	0.33	-0.03	0.74	0.07	0.46	-0.03	0.77	-0.07	0.48	-0.03	0.71
Net EIEE 25 (kcal/min)[bd]	-0.18	0.08	0.07	0.52	0.11	0.27	0.10	0.33	0.04	0.70	-0.02	0.87	0.02	0.87
Net EIEE 50 (kcal/min)[ed]	-0.11	0.23	-0.11	0.24	-0.00	0.96	0.07	0.47	-0.11	0.24	-0.02	0.86	-0.04	0.67

Each coefficient is from a separate regression model. [a]Adjusted for age, sex, and FFM. [b]log transformed. [c]Adjusted for age, sex and BMI. [d]Adjusted for age, sex and FM. [e]outlier excluded

No significant association was found between any PSQI sleep variables and the energy metabolism variables measured.

4.0 Discussion

The aim of the study was to assess the potential association between chronic sleep deprivation/sleep quality and energy metabolism in individuals with obesity. The hypothesis of this master thesis was that chronic sleep deprivation and poor sleep quality was associated with reduced RMR, higher RQ values (reduced fat oxidation) and decreased EiEE in individuals with obesity. The present study did not confirm our hypothesis and no significant association between sleep duration or quality and energy metabolism was found. The only exception was for Net EiEE 25W where a significant positive association was found with sleep duration measured from the armband.

RMR

The lack of association between sleep deprivation and RMR is not in line with findings from a cross-sectional evaluation of a prospective cohort study in 126 participants with obesity (BMI 38.6 +/- 6,5 kg/m2) published by De Jonge with collaborators, who reported that poor quality was associated with increased RMR and increased fasting RQ in individuals sleeping less thant 6.5 h/night (63). De Jonge et al. looked into both sleep duration and quality. REE and RQ were assessed by IC, and sleep duration/sleep efficiency were determined by actipgraph, whereas sleep quality was estimated by PSQI. However, De Jonge et al. investigated both sleep apnea, short sleep, and sleep disturbance. It has to be taken into consideration that both sleep apnea and short sleep are associated with obesity, and individual contribution to the results could not be easily extricated. The increased RMR could be caused by an activation of the stressor system as a result of sleep apnea. In the present study, sleep apnea was an exclusion criteria, even though the participants were not screened for this (self-reported). Further, compared to this present study, De Jonge et al. lacked a control group of non-sleep-deprived individuals with obesity. Furthermore, two thirds of the participants in the study of De Jonge et al. were minorities, compared to the present study where all participants were Caucasian. Sleep restriction could affect EE in different racial groups (52). Another limitation in that study, where that women were examined regardless of their menstrual cycle. Menstrual cycle influences both sleep and RMR (103, 104), and RMR is increased approximately 2 % in the mid luteal phase vs. the early follicular phase (105). Furthermore, sleep time/quality and sleepiness are different in the different phases of the menstrual cycle (103). At last, a small

portion of the individuals in De Jonge et al. study were on various medications, including statins and antihypertensive agents that might have influence on the results.

De Jonge et al. (63) is the only previous public study that has investigated the association between chronic sleep deprivation and RMR and RQ. Most studies that have examined the impact of sleep deprivation on EE have been epidemiological studies investigating the effect of acute sleep deprivation on energy metabolism (37, 40, 45, 49, 52-54, 61, 62), with conflicting findings. The results from this present study are in line with three randomised controlled trials (RCTs), which assessed the effects of partial acute sleep deprivation on RMR (37, 40, 50, 61, 62) without finding any significant effect on RMR. However, it needs to be taken into consideration that the primarily aim of these laboratorial studies was to look into acute sleep deprivation, not chronic sleep deprivation. Both Nedeltcheva et al. (40) and St-Onge et al. (61) measured sleep in a controlled laboratory setting. Nedeltheva et al. enrolled 11 sedentary participants (5 women, 6 men) for two 14 day periods with 5.5-h bedtime vs 8.5-h bedtime, versus St-Onge et al. enrolled 15 men and 15 women in 2 phase of 5 night's sleep period with 4 h/night vs 8 h/night sleep conditions. In the study of St Onge et al., RMR was reduced after a period of 4 nights of short sleep vs. habitual sleep (1455.4 ± 129.0 kcal/d vs. 1486.5 ± 129.5 kcal/d) ($P = 0.136$). In both studies, sleep was measured with PGS and RMR was measured using a ventilated-hood indirect calorimetry system. Both studies enrolled equal number of men and women, young-to-middle adults with normal weight (61) and overweight (40). Furthermore, Bosy-Westphal et al. (62) investigated sleep deprivation after 4 nights of consecutively sleep curtailment from 8 h to 4 h sleep/night. Compared to the above mention studies, in this study all subjects slept at home, and sleep duration was assessed using a 24-hour heart rate monitoring. In contrast, other experimental studies have shown a lower RMR with acute sleep deprivation (45, 52-54). In a study of Spaeth et al. (52), particularly in African Americans men who sleep 4h/night for 5 nights, there was a decrease in RMR after sleep restriction (-2.6%, p=0,03). The participants were not permitted to leave the laboratory during the protocol, and sleep was measured with a wrist actigraph and PSG, where RMR was measured using IC. Spaeth et al. also examined race and gender differences in EE response to sleep restriction and found that African Americans gained more weight and exhibited a lower RMR than Caucasians. Further, Benedict et al. (45) examined 14 normal-weight males in a randomized crossover design with two 24-h conditions. Sleep was measured with PSG, and RMR was measured with IC. In this study, RMR was reduced after one night with sleep

deprivation compared with to one night with regular sleep (8 hours) (5.5 ± 0.1 compared with 5.8 ± 0.2 kJ/min; $P < 0.05$).

These conflicting findings could be due to methodologic differences between the studies. First, the duration of sleep restriction varied from total sleep deprivation (45) to 5.6 h/night (54). Second, the interventions were generally of short duration, with an average of 1-5 nights spent in the sleep deprivation and control conditions, with the longest intervention being 3 weeks per condition (54). It may be possible that the time frame in most of these studies were insufficient to allow for adaptation of the metabolic rate. Third, most studies included participants with normal weight and overweight, only Bosy-Westphal et al. included a few participants with obesity (62). Of the studies that included female participants, only a few accounted for the menstrual phase (40, 62). Furthermore, most studies were conducted in a laboratory setting. A minority were a combination of laboratory setting and free-living, whit only one entirely free-living (62). Sleep deprivation experiments in laboratory have limitations and the generalizability of the findings to a free-living setting is limited (48).

Even though this present study did not find any association between chronic sleep deprivation and RMR, two earlier long-term experimental studies in a controlled laboratory setting support the hypotheses that chronic sleep deprivation and poor sleep quality are associated with reduced RMR (53, 54). Nedeltcheva et al. preformed a 14-day sleep restriction study in 10 overweight (BMI 27.4 +/- 2.0) kg/m2) adults (3 female/7 male) with a hypocaloric diet, which resulted in a reduced and decreased loss of fat when sleep opportunity was restricted to 5.5 h/nigh (53). RMR was lower, and fasting and postprandial RQ higher at the end of the 5.5 h compared to the 8.5-h time-in-bed condition. Additionally, Buxton et al. (54) preformed a 3 weeks sleep restriction study combined with circadian disruption in 21 adults (10 female/11 male), and observed a notable decrease in RMR (-8% on average for all subjects) with prolonged sleep restriction (5.6 h/night). The participants lived in an individual laboratory suite in dim light and without cues, and where served a standardize meal. The results of this study could reveal adaptive or maladaptive physiological effects that emerge beyond the immediate acute metabolic effects observed in the shorter acute sleep restriction studies discussed previously. Furthermore, the combination of sleep restriction and circadian disruption may be qualitatively different than insufficient sleep alone. The prolonged duration of these studies (14 and 3 weeks) are important because they demonstrate that chronic exposure to sleep restriction might contribute to reduction in RMR. However, one should be

cautious to interpret the association observed in these experimental studies. The small number of participants in these studies limit its study power. Larger clinical trials of prolonged duration are needed to determine whether there are a casual association between chronic sleep deprivation and RMR.

In contrast to Buxton et al. (54) who looked into individuals with normal weight (24.2 ± 2.6 kg/m2 vs. 23.3 ± 1.9 kg/m2) and Nedeltcheva et al.(53) who investigated parthicipants with overweight, this present study looked only at individuals with obesity. Most data from sleep restriction studies are in normal or overweight individuals where there is a known association between sleep duration and obesity (9, 15, 17-21). A potential reason for the present findings may be explained by metabolic adaption. Metabolic rate is highly variable in individuals with obesity and literature suggest that metabolic rate may decrease significantly in response to chronic caloric restriction or previous weight loss attempts, resulting in a metabolic rate that is lower than expected in these individuals (106). In this present study, metabolic adaption could already have effected RMR in both groups (both chronic short sleepers (< 7h) and normal/long sleepers (> 7h). More research is needed to determine the role of metabolic adaption in individuals with obesity on EE and cronic sleep deprivation.

Resting RQ

In the present study, there were no significant associations between habitual sleep duration and resting RQ. This finding is not in line with the conclutions from De Jonge et al., which reported that poor sleep and quality was associated with higher RQ (63). However, De Jonge et al. included sleep apnea in the research, and both were associated with increased fasting RQ. Furthermore, eight percent of individuals were smokers and a small portion were on various medications, including statins and antihypertensive agents.

Most studies that have investigated the impact of sleep deprivation on RQ have been laboratorial studies and have looked at the association between acute sleep deprivation and EE (46, 49, 50, 60, 107). Findings from this present study is in line with evidence from several laboratorial studies who looked at the association between acute sleep deprivation and RQ (46, 49, 50, 60, 107). Findings from a 3 night study of Hibi et al. (107) in nine normal weighted men (BMI 22.2 ± 3.0 kg/m^2), indicated that 24h RQ did not differ significantly between sleep conditions, despite the greater number of hours spent awake in the 3.5 h sleep

condition (7h/night vs 3.5h/night. A similar result has been reported by Shechter et al (50), who reported that the 24h RQ after 3 nights of short (4h/night versus 8h/night) sleep duration did not differ significantly under fixed meal conditions. There are also studies that found that sleep restriction significantly decreased fasting RQ. Shechter et al (46) and Klingenberg et al (60) reported a lower fasting RQ after shortened versus habitual sleep. In contrast, there are studies reporting that sleep restriction increases RQ after sleep deprivation (51-53, 63), which has been associated with weight gain (47, 57, 58). Result from a study of Spaeth et al. (52) in 36 participants with 4h sleep/night for 5 nights found that sleep restriction decreased morning RMR and increased RQ in African Americans relative to Caucasians. However, the increase in RQ was also observed in control subjects, suggesting that factors other than sleep restriction, such as overeating and living in a sedentary laboratory environment, contributed to the RQ effect. A 14-day clinical laboratory sleep restriction study by Nedeltcheva and collaborators (53) looked into loss of fat and fat-free body mass and changes in substrate utilization in 10 overweight (BMI 27.4 +/- 2.0) kg/m2) adults (3 female/7 male) under a hypocaloric diet. The result showed reduced EE and decreased loss of fat when sleep opportunity was restricted to 5.5 h/nigh (53). RMR was lower, and fasting and postprandial RQ higher at the end of the 5.5 h compared to the 8.5-h time-in-bed condition. The results showed that sleep restriction decreased the fraction of weight loss as fat by 55 % (1.4 vs 0.6 kg) and increased the loss of fat-free body mass by 60% (1.5 vs 2.4 kg). Nedeltcheva and collaborators concluded that the amount of sleep could contribute to the maintenance of fat-free body mass at times of decreased EI. This is also supported by other studies showing that that better sleep quality and greater sleep was associated with greater FM loss (59, 108). However, these studies did not measure RQ.

Studies examining the impact of sleep deprivation on RQ have produced disparate results. These conflicting results are likely due to differences in participants characteristics and study design. A limitation in the study of Hibi et al. (107) was the normal sleep condition of 7 h pr night, which may be considered a mild sleep disturbance compared to studies providing 8 or 9-h sleep opportunities (46, 52, 53, 60). Another limitation comparing acute sleep studies with chronic sleep deprivation is that the results only partly resemble real life, because of the clinical setting (46, 49, 63, 107). Moreover, small sample sizes, few individuals with obesity, short duration, and different macronutrient composition of diet and distribution of energy makes it difficult to detect differences between sleep periods. However, other determinants such as genetic, gender, energy balance, overeating, insulin sensitivity, circulating insulin and

sedentary lifestyle, could also contribute to elevated RQ (91, 109). In the present study, the participants had the freedom to eat what they desired to eat, with the only restriction being to abstain from caffeine for at least 6 hours before testing and to avoid alcohol consumption 24 h before testing. Food intake (amount of food) and nutrient balance, have a major effect on fat oxidation, which potentially could have had an impact on RQ measured in this present study, compared to other studies with restriction in choice and amount of food.

EiEE

The present study did not find any association between sleep duration (arm bands and PSQI) and Net EIEE 10W or Net EiEE 50W, nor between sleep quality (PSQI) and Net EIEE 10W or Net EiEE 50W. However, there was a positive significant association between Net EIEE 25W and sleep duration from the armbands.

No previous literature examining sleep deprivation in individuals with obesity and Net EIEE seems to exist. Moreover, differences in intervention and protocol used to measure EIEE (stationary bike versus treadmill, different resistances, speed and inclinations) makes comparisons to other studies difficult. In the present study there was a small positive correlation between sleep duration from arm bands and sleep duration from PSQI ($r = 0{,}25$, $^{*}P = 0.04$). One of the reasons for the correlation may be that the arm band reflects a more recent past, while the PSQI reflects sleep duration over the last year. That may explain the significant findings for the sleep duration when information from armbands was used (sleep duration the last week before data was collected), but not from the PSQI. It remains to be discovered the reason behind the fact that one only detected a positive significant association between sleep duration from the armbands and Net EIEE at 25W but not at other power levels. More studies are needed in this area.

A significant positive association between Net EiEE and sleep duration indicates that reduced sleep leads to decreased energy-cost during exercise. If not compensated by more activity or lower EI, decreased energy-cost could cause people to gain weight However, several other mediating factors like impaired muscle metabolism, reduced habitual daily physical activity and cardiac dysfunction might partly explain this decreased energy-cost. Additional randomized controlled studies are needed to better understand the connection between sleep deprivation in individuals with obesity and EE.

Studies examining the impact of sleep duration and quality on energy metabolism could have produced disparate result due to differences in sleep protocols and measurement types. In the present study, the participants experienced a relatively moderate degree of sleep restriction (6.5 h/night (6, 7.2) from armband, 6.7 ± 1.0 h/night from PSQI), compared to the recommended optimal sleep duration (7-9 hours). In contrast, most laboratory findings are from studies with restricted sleep to 4-5 h/night (52-54, 61, 110). Current sleep recommendations suggest that a generalized optimum sleep duration exist for the population (between 7 and 9 hours for adults) (75-77). According to specific health outcomes it is possible that different optimal sleep durations exist (75). There is also inter-individual variability in sleep needs, and likely that there are "short sleepers" in the natural environment ("short sleepers" without sleep insufficiency), as well as "short sleepers" with varying levels of sleep insufficiency. A sleep duration range implies that there is a U-shaped relationship between sleep duration and health outcomes. For instance, in the Nurses' Health Study (111), women sleeping <5 h per night displayed the highest degree of body weight, whereas a sleep duration of 7-8 h was associated with the lowest degree of body weight (111). While short sleep is consistently associated with adverse health outcomes, long sleep is generally associated with lower adiposity indicators, better emotional regulation, better academic achievement, and better quality of life/well-being (18). The term of habitual sleep duration is described differently between studies, some define short sleep as less 6 h/night and some use <7 h/night. This might be one factor explaining the conflicting findings between this present study and previous research looking at sleep deprivation and EE.

It is important to take into consideration that a reduction in EE after sleep deprivation could also result from decreased PA. Some individuals may reduce their spontaneous PA levels or even increase their sedentary behaviour after sleep deprivation, as a cause of fatigue and tiredness (51, 62, 112, 113). It has been observed large inter-individual variation in PA after sleep restriction, with some individuals reporting increased PA (113) and some no association between sleep deprivation and PA levels. In this study, the participants average PAL was 1.2 and the average moderate PA was under 1h/day (57.8 ± 38.9). However, it did not investigate a potential association between habitual sleep duration or sleep quality and PA, as par.

Another considerable fact is that sleep deprivation can affect EI and endocrine regulators of energy balance. There is robust evidence showing that increased food intake as a result of

insufficient sleep is the main explanation to the association between sleep deprivation and weight gain/obesity. Many studies have reported an increase in ad libitum food intake after loss of sleep (40, 61, 62, 113, 114) and increased EI of snacks in particular (40). Acute sleep deprivation is also associated with increased EI trough deregulated appetite (increased hunger feeling and decreased feeling of fullness) (22, 40, 61, 113). A systematic review and meta-analysis of intervention studies suggested that partial sleep deprivation may lead to a net positive energy balance of 385 kcal per day because a significant increase in total 24-h EI, and no effect on 24-h EE (37). However, the results were mainly based on studies with highly restrictive sleep schedules conducted in controlled laboratory conditions over a short period of time (1 day to 2 weeks). It remains unknown whether the observed net positive energy balance is evident over a prolonged period of less restrictive sleep deprivation that mirrors the effect of chronic sleep debt. Although studies suggest that restricting sleep may lead to weight gain via increased food intake, more research is needed to examine its long term impact on EE.

In summary, no significant correlation was found between sleep deprivation or sleep quality and RMR, RQ and NET EIEE, except for a positive correlation between NET EIEE 25W and sleep duration from the arm bands. There is a strong epidemiological evidence that sleep deprivation is associated with weight gain and obesity at the population level (15, 23, 26). However, the exact reasons for this remains to be explored. A reduction in EE because of chronic sleep deprivation may initiate a mechanism that, along with decreased PA (8) and an increased food intake (6) after sleep deprivation, may strengthen the association between chronic sleep deprivation and obesity. Daily EE is largely determined by body size, and any effects on weight change would be expected to require several years of follow-up to be observed. Further long-term studies investigating the effects of chronic sleep deprivation in individuals with obesity are required to understand the link between sleep and the energy metabolism.

Methodical discussion

In the present study, PSQI was used as a subjective measure in both duration and quality of sleep. Additionally, SenseWear armband was used as an objective measure of sleep duration alongside PSQI. PSQI is one of the most widely used health-assessment tool in both clinical and non-clinical populations and its validity and reliability have been widely confirmed (99).

It is known to distinguish between people with regular sleeping patterns and those who have sleeping problems fairly accurately (99). PSQI is cost-effective and easy to administer and has high patient compliance. One advantage of using this screening tool is to assess important components of subjective sleep quality. However, it is a subjective measure of sleep duration/quality and self-reporting bias might therefore occur.

Furthermore, SenseWear armband was used as an objective measure of sleep duration. Even though PSG is currently considered the gold standard for measuring sleep, it has been suggested that when assessing sleep in individuals with obesity, a combination of artigraphs and subjective methods, such as PSQI may perform better than PSG (115). PSG requires participants to sleep overnight in a laboratory setting, which may disrupt normal sleep patterns (115). Furthermore, the technique is expensive, time consuming and not ideal for large sample size. Actigraphs and subjective sleep measures, such as PSQI are hence preferable and more suitable for use in the field, as they can measure habitual sleep patterns and quality over a longer time period (115). Additionally, the participant can sleep at home and engage in normal daily activities and therefore provide a more realistic sleep patterns compared with PSG. SenseWear arm bands are gaining popularity and recognition in epidemiological research (22,23) and have been used to measure sleep duration in individuals with obesity in other studies (119). However, actigraphs can be less accurate in individuals who experience disturbed sleep compared with PSG. SenseWear arm band has low specificity in detecting wake during night and might overestimate total sleep time (115, 116). Therefore, no objective measure of sleep quality was available in this study.

IC was used to measure RMR, RQ and EiEE. IC is seen as the gold standard for measuring EE and as a validated and accurate method to use in clinical settings (117). IC provides sensitive, accurate, and non-invasive measurements of all components of EE and is the most accurate assessment tool for individuals with obesity (85, 118). It is important to consider that measurement of respiratory gases is only accurate and reliable when conducted under standard resting conditions, and certain procedures in the inpatient setting may affect the oxygen dynamics and accuracy of IC (118). In this present study, standardized procedures were followed to obtain accurate and reliable results (101, 117).

The association between habitual sleep duration/quality and the metabolic components was assessed by multiple regression analysis after adjusting for potential confounders (age, sex,

FFM, FM BMI). It cannot be excluded that other important confounders, not accounted for in the statistical analysis exist, which could have distorted the findings.
Furthermore, this was a cross-sectional study. Cross-sectional studies have potential for sampling bias and must be treated carefully. Compared to randomized controlled trials, which is considered the gold standard, observational studies can be influenced by known and unknown confounding variables and therefore a cause-effect relationship cannot be established.

4.1 Strengths and limitations

4.1.1 Strengths

This present study has several strengths. First, several components of EE were measured using gold standard validated methods. Second, sleep duration and sleep quality have been measured using both subjective and objective methods (PSQI and SenseWear armbands). Third, this study included both males and females in almost similar numbers (55% females). Additonally, it was adjusted for potential confounders.

4.1.2 Limitations

This study also has some limitations. First of all, this study is unpowered. It is possible that a larger study with individuals with obesity could have detected an association between sleep duration/quality and RMR, RQ and EiEE with a significant sex interaction. Second, the phase of menstrual cycle was not taken into consideration. Female menstrual cycle influences many parameters, including RMR (104) and sleep (103). Third, since all individuals in this present study are obese, metabolic adaptations in RMR are likely to be present in both groups of participants presented (sleeping over/under 7 hours), due to earlier treatments for obesity and previous weigh loss attempts. Additional potential limitations are the population in this study. The sample is Caucasian (Norwegian) with obesity, which may limit the generalizability to other populations.

4.2 Future research

Short sleep-time and sleep disturbance might lead to changes in individual energy balance and may increase the risk of obesity. Most studies on the impact of sleep deprivation on EE have been in a laboratory setting and have used an acute sleep loss model. Cross-sectional and longitudinal epidemiological studies show a relationship between sleep deprivation and increased prevalence of obesity and weigh gain. However, causality cannot be inferred from such studies. More and longer clinical intervention studies with larger samples of individuals are needed, looking at partial sleep deprivation which mirrors real life scenarios to further investigate the association between chronic sleep deprivation and energy metabolism

5.0 Conclusion

No association seems to exist between habitual sleep quality or duration and RMR or FatOx. There might be a positive association between habitual sleep and EIEE. RCT evaluating the impact of chronic sleep deprivation on energy metabolim in individuals with obesity are needed.

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Forespørsel om deltakelse i forskningsprosjektet

Hvordan holde vekten etter diettindusert vekttap?

Bakgrunn og hensikt

Dette er et spørsmål til deg om å delta i en forskningsstudie med utgangspunkt i en 8-ukers streng diett etterfulgt av ett års oppfølging med sikte på å stabilisere vekten. Problemsstillinger i studie er:

- Er de ulike oppfølgingsprogrammene like gode?
- Hvordan påvirkes hormonene som regulerer appetitt i diettens aktive fase?
- Hvordan påvirker tarmens bakterieflora kroppsvekten etter en vektreduksjons fase?
- Hvordan påvirker fedme og vektreduksjon immunologiske og homeostatiske mekanismer i relasjon til aterosklerose
- Hvordan påvirker vekttap beintetthet og markører for beinomsetning

Det er St. Olavs Hospital som er ansvarlig for studien.

Hva innebærer studien?

Studien er delt i to faser. Den første fasen er en 8-ukers diettperioden, etterfulgt av 4 uker med vekt vedlikehold, som vil være den samme for alle som deltar. En slik lavkalorikur kan gi noen bivirkninger (beskrevet senere). Når dietten er overstått vil du gå over i studiens andre fase som dreier seg om oppfølging med sikte på å opprettholde vekttapet.

Halvparten av pasientene vil få oppfølging i Fedmepoliklinikken ved St. Olavs Hospital, mens den andre halvparten får oppfølging ved Røros Rehabilitering. Hvilken oppfølging du får er avhengig av hvor det er kapasitet for oppfølging på tidspunktet du inkluderes i studien. Oppfølgingen varer i ett år og du kan lese mer om den på neste side.

Undersøkelsene er de samme uansett hvilket oppfølgingsprogram du følger og innebærer blodprøver, blodtrykk, målinger av energibehov, kroppsmasse, DXA (dual X-ray absorbiometry) skanning til å måle beintetthet og oksygenopptak, samt ulike former for spørreskjema.

Mulige fordeler, ulemper og bivirkninger

Fordelen med studiedeltakelse kan være at man går ned i vekt og oppnår bedre helse uten kirurgisk behandling. Deltakelse kan også gjøre at du blir bedre kjent med mekanismene i din egen kropp som påvirker appetitten. Dessuten vil du spare kostnader til mat i studiens diettfase (diettproduktene får du gratis ved sykehuset). Behandlingen anses ikke som risikabel. Undersøkelsene innebærer noen blodprøver.

Lavkalorikurer kan ha flere bivirkninger. Omfanget av disse varierer fra person til person og kan være enten helt fraværende eller temmelig plagsomme. Bivirkninger er forbigående. Rapporterte bivirkninger er:

- slapphet
- svimmelhet
- forstoppelse
- hårtap
- tørr hud
- neglene kan bli sprøere
- kvalme

- diaré
- forstyrret menstruasjonssyklus
- økt kuldefornemmelse

Beintetthet i rygg og hofte vil måles med DXA (dual X-ray absorbiometry) skanning. Dette er en smertefri og rask lavdose røntgenundersøkelse. Mengden stråling ved DXA er mindre enn en tiendedel av dose ved et standard røntgenbilde av brystet, og mindre enn mengden av naturlig stråling du blir utsatt for.

Hva skjer med prøvene og informasjonen om deg?

Prøvene tatt av deg og informasjonen som registreres om deg skal kun brukes slik som beskrevet i hensikten med studien. Alle opplysningene og prøvene vil bli behandlet uten navn og fødselsnummer eller andre direkte gjenkjennende opplysninger. En kode knytter deg til dine opplysninger og prøver gjennom en navneliste. Noen helseopplysninger vil også lagres i din pasientjournal, og disse vil være knyttet til ditt personnummer.

Det er kun autorisert personell knyttet til prosjektet som har adgang til navnelisten og som kan finne tilbake til deg. Det vil ikke være mulig å identifisere deg i resultatene av studien når disse publiseres.

Frivillig deltakelse

Det er frivillig å delta i studien. Du kan når som helst og uten å oppgi noen grunn trekke ditt samtykke til å delta i studien. Dette vil ikke få konsekvenser for din videre behandling. Dersom du ønsker å delta, undertegner du samtykkeerklæringen på siste side. Om du nå sier ja til å delta, kan du senere trekke tilbake ditt samtykke uten at det påvirker din øvrige behandling. Dersom du senere ønsker å trekke deg eller har spørsmål til studien, kan du kontakte studiekoordinator Hege Bjøru, telefon 40 87 34 24.

Studien er godkjent av Regional komité for medisinsk og helsefaglig forskningsetikk REK Midt-Norge.

Ytterligere informasjon om studien finnes i kapittel *A* – *utdypende forklaring av hva studien innebærer.*
Ytterligere informasjon om personvern og forsikring finnes i kapittel B – *Personvern, biobank, økonomi og forsikring.*

Samtykkeerklæring følger etter kapittel B.

Kapittel A – Utdypende forklaring av hva studien innebærer

Kriterier for deltakelse

De som kan delta i denne studien må

1. ha BMI mellom 35 og 45 kg/m^2,
2. være mellom 18 og 65 år,
3. ha et ønske om å gå ned i vekt ved hjelp av diett,
4. være relativt vektstabil siste tre måneder

Kvinner må dessuten enten være over menstruerende alder eller benytte p-piller.

Mange kan ha forsøkt dietter tidligere og du bør derfor tenke deg godt om hvorvidt dette er en behandling som er verdt å forsøke igjen. Hvis dette føles galt, så bør du ikke ta del i studien.

Bakgrunn for studien

Lavkaloridietter (< 800 kcal/dag) er en relativt sikker metode for å gå ned i vekt og gir også et raskt vekttap. Slike dietter kan gi vekttap i størrelse 10-15 % og med det også bedring i overvektsrelaterte sykdommer og risikofaktorer. Langtidseffektene er imidlertid usikre og særlige utfordringer er knyttet til opprettholdelse av vekttap på sikt. Det er behov for mer kunnskap om diettens vedlikeholdsfase, spesielt knyttet til tidspunktet man går over fra diettprodukter til mer normal, energiredusert kost.

Hovedhensikt med denne studien er å sammenligne opprettholdelse av vekttap etter 8-ukers lavkaloridiett hos pasienter som deltar i to ulike oppfølgingsprogram. Oppfølgingen varer i ett år.

Vi vil også se nærmere på hvordan den hormonelle appetittreguleringen endres i diettens aktive fase. Appetitten er et komplisert samspill av blant annet hormoner som både stimulerer og reduserer matlysten og vi vil følge utviklingen i disse i løpet av de ukene dietten varer. Det er hittil gjort lite forskning på dette.

Undersøkelser

Som del av studien vil du gjennomgå ulike undersøkelser.

- Veiing og kroppsmassemåling
- Blodtrykksmåling
- Blodprøver
    - Måling av appetitthormoner og ketone kropper (72ml)
    - Testing for kjente gener som disponerer for fedme (3ml)
    - Måling av immun og homeostatiske mekanismer (25ml)
    - Måling av markører for beindannelse og beinnedbrytning (3ml)
- Indirekte kalorimetri (måling av energibehov)
- Måling av oksygenopptak
- Spørreskjema
- Avføringsprøver
- Måling av beintetthet i hofte og ryggrad med DXA (dual X-ray absorbiometry) skanning

Undersøkelsene finner sted ved studiens start, ved avslutning av dietten (uke 9), etter fire uker av vekt holdning (uke 12) og ved avslutning av oppfølgingen (etter ett år).

Tidsskjema for intervensjonperioden (12 uker) - felles for alle

Du vil få utdelt et variert utvalg av diettprodukter (milkshakes, smoothies, supper) tilsvarende et daglig energiinntak på 550 kcal (kvinner) og 660 kcal (menn). Du skal utelukkende spise disse produktene mens du er i diettens aktive fase (8 uker) (standardisert for alle), men du oppfordres til å drikke rikelig (minst 2,5 liter) vann og evt kalorifri drikke i tillegg. Du vil så få time hos en sykepleier i Fedmepoliklinikken hver uke. Kostdagbok, veiing og urinprøver er del av denne fasen og bivirkninger rapporteres systematisk. I studieuke 9 får du time hos klinisk ernæringsfysiolog som vil foreskrive en ny diett av normalkost som du skal følge i året som kommer med sikte på å opprettholde vekttapet.
Overgangen fra diettprodukter til normalkost skjer gradvis i løpet av studieuke 9 og 10.

Tidsskjema for deltakere ved Røros Rehabilitering (1 år) - halvparten av deltakerne

For de som trekkes ut til å delta på Røros Rehabilitering, innebærer deltakelse tre opphold ved Røros. Hvert opphold varer i tre uker og gjøres unna i løpet av ett år. Oppholdene innebærer mye fysisk aktivitet, oppfølging av helsepersonell både individuelt og i grupper, samt matlaging i fellesskap. Mer informasjon og tidsplan for oppholdene vil bli distribuert senere.

Tidsskjema for deltakere ved Fedmepoliklinikken (1 år) - halvparten av deltakerne

For de som trekkes ut til å delta i Obesitaspoliklinikkens program, innebærer det en individuell konsultasjon hos klinisk ernæringsfysiolog og senere gruppemøter med ulike helsepersonell. Gruppemøtene finner sted 3, 6, 9 og 12 mnd etter dietten og fokuserer mye på ernæring og fysisk aktivitet.

Studiedeltakerens ansvar

Det er studiedeltakerens ansvar å møte til avtalt tid. For de som deltar ved Røros Rehabilitering, må de påregne å være der gjennom hele treukersperiodene.

Kompensasjon og egenandel

Det gies ingen premiering for å delta i studien, men du vil få diettproduktene i diettens aktive fase gratis. Det er viktig å standardisere dietten slik at alle spiser det samme.

For deltakere ved Røros Rehabilitering vil fastlegen gi sykmelding for perioden oppholdene varer. NAV innvilger i de aller fleste kommunenes tilfelle også fritak for arbeidsgiverperioden, men det er også noen kommuner som ikke gjør dette pr i dag.

For deltakere ved Røros Rehabilitering vil det også tilkomme egenandel. Denne dekker behandling, kost og losji og betales inntil man når beløpsgrensen for Frikort 2. (Beløpsgrense fastsettes av myndighetene fra år til år.)

Kapittel B – Personvern, biobank, økonomi og forsikring

Personvern

Ulike opplysninger vil registreres om deg som del av dette prosjektet. Prøvesvar og innledende screeningnotat vil legges i din pasientjournal og er derfor personidentifiserbart. Opplysninger på bakgrunn av testene du gjennomgår og intervjuet vil lagres på sykehusets server og vil være avidentifiserte så lenge studien pågår (det vil si at et unikt ID-nummer erstatter navnet ditt). Kodenøkkelen som knytter navn til nummer makuleres når studien er slutt, slik at data da anonymiseres. Alle som jobber med data fra studien har taushetsplikt.

Vi vil benytte et internettbasert system for å samle spørreskjemadata. Dette betinger at du har tilgang til en datamaskin eller smartphone. Rapporteringssystemet krypterer dine svar slik at det ivaretar kravene til personvern.

St. Olavs Hospital ved administrerende direktør er databehandlingsansvarlig.

Biobank

Blodprøvene for analyser av appetitthormoner og mulige fedmegener som blir tatt vil bli lagret i en forskningsbiobank ved St. Olavs Hospital. Hvis du sier ja til å delta i studien, gir du også samtykke til at det biologiske materialet og analyseresultater inngår i biobanken. Overlege Bård Kulseng er ansvarshavende for forskningsbiobanken. Det biologiske materialet kan bare brukes etter godkjenning fra Regional komité for medisinsk og helsefaglig forskningsetikk (REK).

Rett til innsyn og sletting av opplysninger om deg og sletting av prøver

Hvis du sier ja til å delta i studien, har du rett til å få innsyn i hvilke opplysninger som er registrert om deg. Du har videre rett til å få korrigert eventuelle feil i de opplysningene vi har registrert. Dersom du trekker deg fra studien, kan du kreve å få slettet innsamlede prøver og opplysninger, med mindre opplysningene allerede er inngått i analyser eller brukt i vitenskapelige publikasjoner.

Økonomi

Studien finansieres over driften ved St. Olavs Hospital og Røros Rehabilitering. Diettproduktene for deltakerne er gitt av produsenten.

Forsikring

Studiedeltakerne omfattes av Norsk pasientskadeforsikring, jf. pasientskadelovens §1.

Informasjon om utfallet av studien

Publikasjoner på bakgrunn av studien vil bli lagt ut på vår hjemmeside, www.stolav.no/overvekt .

Samtykke til deltakelse i studien

Jeg er villig til å delta i studien

(Signert av prosjektdeltaker, dato)

Jeg bekrefter å ha gitt informasjon om studien

(Signert, rolle i studien, dato)

PSQI

Instruksjoner: Følgende spørsmål har med ditt vanlige søvnmønster *den siste måneden* å gjøre. Du skal svare på hva som er mest riktig for *de fleste* dager og netter den siste måneden. Vennligst svar på alle spørsmål.

1. I løpet av den siste måneden, når har du vanligvis lagt deg om kvelden?
   VANLIG LEGGETID_____

2. I løpet av den siste måneden, hvor lang tid (i minutter) har det vanligvis tatt deg å sovne om kvelden?
   ANTALL MINUTTER_____

3. I løpet av den siste måneden, når har du vanligvis stått opp om morgenen?
   VANLIGVIS STÅTT OPP KL_____

4. I løpet av den siste måneden, hvor mange timer søvn har du *faktisk* fått om natten? (Dette kan være forskjellig fra hvor mange timer du oppholdt deg i sengen.)
   ANTALL TIMER SØVN HVER NATT _____

For hvert av de følgende spørsmål, kryss av for det beste svar. Vennligst svar på *alle* spørsmålene.

5. I løpet av den siste måneden, hvor ofte har du hatt problemer med søvnen fordi du…

(a) Ikke klarer å sovne i løpet av 30 minutter

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(b) Våkner opp midt på natten eller tidlig om morgenen

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(c) Må opp for å gå på toalettet

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(d) Ikke klarer å puste ordentlig

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(e) Hoster eller snorker høyt

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(f) Føler deg for kald

Ikke i løpet av den s iste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(g) Føler deg for varm

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(h) Har vonde drømmer

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(i) Har smerter

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(j) Andre grunner, vennligst beskriv_____

_____

Hvor ofte, i løpet av den siste måneden, har du hatt problemer med søvnen på grunn av dette

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

6. I løpet av den siste måneden, hvordan vil du bedømme søvnkvaliteten din totalt sett? Veldig bra _____
   Ganske bra Ganske dårlig Veldig dårlig

7. I løpet av den siste måneden, hvor ofte har du tatt medisin (med eller uten resept) som hjelp til å sove?

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

8. I løpet av den siste måneden, hvor ofte har du hatt problemer med å holde deg våken under bilkjøring, måltider eller når du holder på med sosiale aktiviteter?

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

9. I løpet av den siste måneden, hvor stort problem har det vært for deg å ha overskudd nok til å få ting gjort?
   Ikke noe problem i det hele tatt _____
   Bare et lite problem _____
   Et visst problem _____
   Et stort problem _____

10. Deler du seng eller rom med noen?
    Deler ikke seng eller rom med noen _____
    Partner/romkamerat i annet rom
    Partner i samme rom, men ikke i samme seng Partner i samme seng

Hvis du har en partner eller romkamerat, spør han/henne hvor ofte i løpet av den siste måneden du har hatt…

(a) høy snorking

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(b) lange pustestopp under søvnen

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(c) rykninger eller sammentrekninger i beina under søvnen

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(d) episoder med desorientering eller forvirring under søvnen

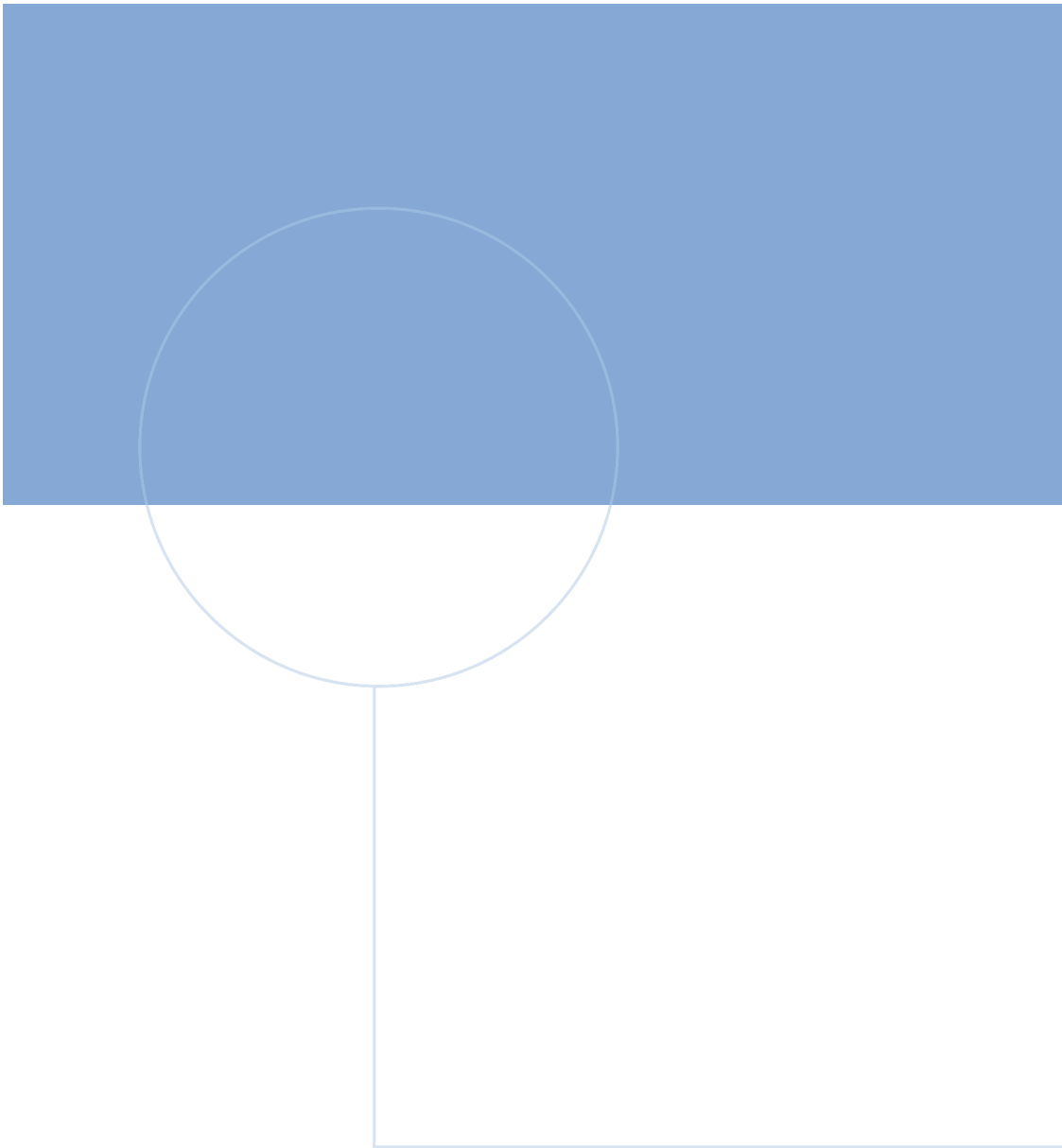
Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uken___

(e) annen type uro under søvnen; vennligst beskriv_____

_____

Ikke i løpet av den siste måneden___	Mindre enn en gang i uken___	En eller to ganger i uken___	Tre eller flere ganger i uke

Pittsburgh Sleep Quality Index
(Buysse, Reynolds III, Monk, Berman & Kupfer, 1989)
Til norsk ved Petter Franer, Inger Hilde Nordhus, Ståle Pallesen og Simen Øverland



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Norwegian University of
Science and Technology