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A study of the link between partial sleep deprivation and obesity

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Table of Contents

I. Abstract 1

II. Introduction 2

III. Preliminary Research 6

IV. Methods 10

V. Results 14

VI. Discussion 15

VII. Conclusion 25

VIII. References 26

Figures

Description	Page Number
Figure 1: Percent difference in levels of leptin and ghrelin comparing short sleep to longer sleep conditions from two studies	7
Figure 2: Curvilinear relationship between BMI and average nightly sleep	8
Figure 3: Changes in BMI with Sleep Duration	14

Abstract

Obesity has become a major health problem with increasing prevalence and is related to multiple medical consequences, such as increased risk for diabetes, heart disease, arthritis, and cancer (Hasler *et al*., 2004). Due to the limited availability of effective treatment of weight problems, it is necessary to identify potential risk factors for obesity. One factor that has received increased attention is chronic partial sleep deprivation (<7 hours of sleep a night). The decrease in average sleep duration over the past three to four decades has occurred simultaneously with the increase in the prevalence of obesity. Chronic partial sleep deprivation could be a possible risk factor for obesity, but current understanding of the processes linking sleep deprivation to obesity is incomplete. The research will focus on examining the possible pathways through which partial sleep deprivation contributes to the development of obesity: alterations in metabolic pathways and waking behavior, including eating behavior and physical inactivity. The hypothesis behind the proposed study is that increasing sleep duration in obese individuals who experience partial sleep deprivation will lead to a decreased BMI. Research addressing the possible pathways and targeting the amount of sleep will benefit individuals in preventing and/or treating obesity.

Introduction

Obesity is defined as having a body mass index (BMI) that is greater than or equal to 30 (Singh *et al*., 2005). BMI is weight in kilograms divided by the square of the height in meters – kg/m^2 (Gangwisch *et al*., 2005). According to the National Health and Nutritional Examination Survey, an estimated 13.4% of adult men and women were obese in 1960, and that percentage of obese adults increased to 30.5% by 2000 (Singh *et al*., 2005). Obesity is a major health problem, as it contributes to conditions such as diabetes, cardiovascular disease, osteoarthritis, and some metabolic-related disorders (Kopelman, 2000). Besides the several factors that may cause obesity, such as high fat diets and sedentary lifestyles, one other factor to consider is sleep deprivation.

Over the past decade, the rise in obesity has occurred along with a reduction in sleep time. The decline in sleeping time is a trend that has become highly prevalent in American society. Today, more than 30% of adult men and women between the ages of 30 and 64 years report sleeping less than 6 h per night (Knutson and Van Cauter, 2008). In addition, a poll conducted by the National Sleep Foundation showed that American adults sleep on average 6 h 40 min during weekdays and 7 h 25 min during the weekend, while in 1960 they slept on average 8.5 h (Leproult and Van Cauter, 2010). Some individuals voluntarily limit the amount of hours they sleep in order to meet work, social, or family demands, and others engage in certain behaviors, such as cigarette smoking and alcohol consumption, that have an impact on sleep duration. In addition, health conditions, medication use, or a low socioeconomic status may be what lessens sleep duration.

Sleep deprivation is a complete lack of sleep during a certain period of time or a shorter-than-optimal sleep time (Orzeł-Gryglewska, 2009). The average basal need is 7 to 8 hours per

night (Colten and Altevogt, 2006). Complete absence of sleep over long periods of time is impossible for humans, meaning total sleep deprivation is necessarily short term and of questionable long-term clinical implications. Therefore, the more recent focus is on chronic partial sleep deprivation (<7 hours of sleep a night) (Colten and Altevogt, 2006). Since the common causes of chronic partial sleep deprivation are those related to modern lifestyle and work, the condition affects a considerable number of people. The common practice of reducing sleep time is driven largely by a greater reliance on longer work hours, shift work, and greater access to television and the Internet (Colten and Altevogt, 2006). Sleep loss, leading to disruption of the sleep cycle, affects every aspect of day-to-day living, such as mood, mental alertness, work performance, and energy level (Epstein, 2007). Most importantly, it can have severe health consequences, specifically a negative effect on appetite regulation.

Sleep is a necessary and natural behavior, yet scientists do not fully understand the functions of sleep (Rechtschaffen, 1998). It has been hypothesized that some of the roles of sleep may be restoration and recovery of body systems, energy conservation, memory consolidation, brain development, and discharge of emotions (Rechtschaffen, 1998). Meanwhile, the physiological changes that occur in the brain and body during sleep have been identified, and they include changes in brain activity, blood pressure, heart rate, and body temperature (Colten and Altevogt, 2006). These changes depend on the specific stage of sleep.

Sleep is an active process and a highly organized sequence of events that follows a regular program each night. Sleep is typically divided into two states – rapid eye movement (REM) and non-rapid eye movement (NREM) (Colten and Altevogt, 2006). REM sleep accounts for 20 to 25 percent of sleep in adults (Colten and Altevogt, 2006). It is characterized (as the name suggests) by rapid eye movements, which occur under closed eyelids. Muscles other than

eye and breathing muscles do not move during this stage of sleep. NREM sleep, on the other hand, constitutes about 75 to 80 percent of total sleep and is subdivided into stages 1, 2, 3, and 4, representing a continuum of relative depth (Colten and Altevogt, 2006). Each stage has different characteristics, including variations in brain wave patterns, eye movements, and muscle tone. Sleep is also a cyclic process, as REM sleep alternates with NREM sleep. People experience repeated cycles of NREM and REM sleep, beginning with NREM sleep. These cycles last about 90 to 120 minutes and are repeated multiple times per night (Colten and Altevogt, 2006). The function of these sleep alternations is unknown, but irregular cycling and/or absent stages are associated with sleep disorders (Zepelin *et a*l., 2005).

The four stages of NREM sleep are as different from one another as sleeping is from waking. During Stage 1 of NREM sleep, the predominant brain waves slowdown from eight to twelve cycles to four to seven cycles per second (Epstein, 2007). The body temperature decreases, the muscles become relaxed, and the eyes move slowly from side to side. People in Stage 1 can be easily awakened. Once they are in Stage 2, they have reached the first stage of established sleep. The first time it occurs, it lasts ten to twenty-five minutes before progressing to the next stage (Epstein, 2007). A characteristic of this stage is irregular electrical activity in the brain. The sleeper has brief bursts of fast activity, called sleep spindles, and a pattern called a K-complex, or a built-in vigilance system in order for the person to wake up if necessary (Epstein, 2007). Stages 3 and 4 are referred to as slow-wave sleep (SWS) (Colten and Altevogt, 2006). As the person goes into deeper sleep, the resulting waves become bigger. These large slow brain waves are called delta waves and at least half of them are present when the person is in Stage 4 (Epstein, 2007). By this stage, it is difficult to be awakened by external stimuli.

Sleep influences two major hormones that play a major role in appetite regulation, leptin and ghrelin, Leptin is a satiety hormone secreted by the adipocytes, and ghrelin is an appetite-stimulating hormone released primarily from stomach cells (Leproult and Van Cauter, 2010). Thus, they exert opposing effects on appetite. Because leptin depends mainly on meal intake, there are lower levels in the morning times and increasing levels throughout the day, leading to higher levels at night (Leproult and Van Cauter, 2010). Even so, a study using continuous enteral nutrition that eliminated the impact of meal intake showed the persistence of a sleep-related leptin elevation (Simon *et al*., 1998). Leptin may be elevated at night to inhibit hunger during the overnight fast. Ghrelin levels decrease rapidly after the ingestion of meals and increase after 1.5 - 2 hours with the resurgence in hunger (Knutson and Van Cauter, 2008). For example, ghrelin levels would increase at night due to a post-dinner rebound. However, they decrease during the second part of the night, even though there is no food intake (Leproult and Van Cauter, 2010), which suggests that sleep has an inhibitory effect. The effect of sleep on both leptin in ghrelin is important in the link between sleep deprivation and obesity.

In addition to altering hormone levels in the body, sleep may also influence food intake and energy expenditure. Both sides of the energy equation (energy intake and energy expenditure) are important to understanding the processes through which sleep deprivation promotes obesity. According to the concept of energy balance, obesity develops if energy intake, in the form of feeding, chronically exceeds total body expenditure (Spiegelman and Flier, 2001). Energy expenditure takes the form of physical activity, basal metabolism, and adaptive thermogenesis. Physical activity is all voluntary movement, while basal metabolism refers to the biochemical processes needed to sustain life, and thermogenesis refers to energy dissipated as heat in response to changes in the environment (Spiegelman and Flier, 2001). Nedeltcheva *et al*.

was the first study to measure the effect of sleep restriction on the components of human energy intake and expenditure (2009). There was an increased consumption of calories from snacks, while energy expenditure remained unchanged with sleep restriction (Nedeltcheva *et al*., 2009). Conversely, Schmid *et al.* showed that sleep restriction led to a reduction in physical activity under free-living conditions, but no significant changes were found in food intake, hunger and appetite, and levels of leptin and ghrelin (2009). Further investigation in studies that examine whether sleep deprivation alters energy expenditure or its components is necessary.

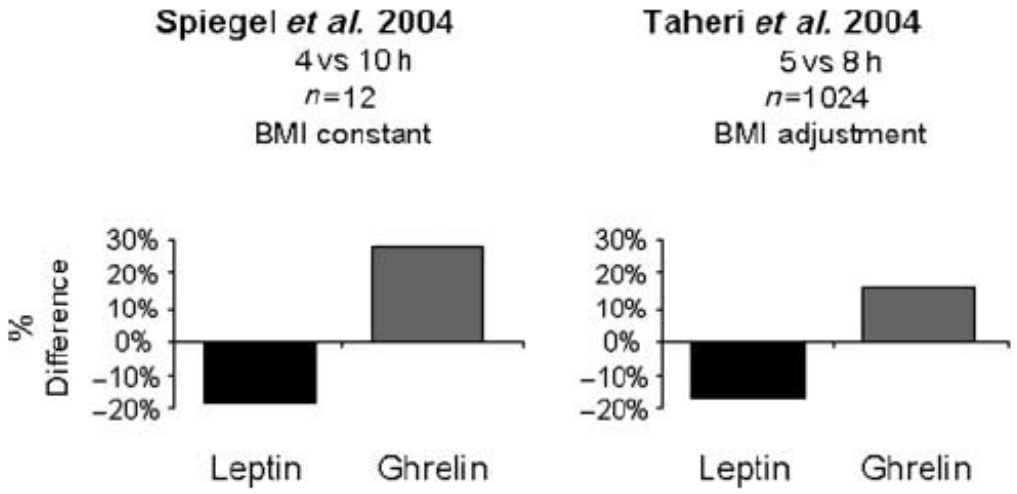
The way in which sleep deprivation interacts with body weight, contributing to obesity, is unknown (Taheri *et al*., 2004). If sleep deprivation is targeted as a modifiable risk factor for obesity and weight gain, there is a need to better understand the pathways linking sleep deprivation to obesity. Sleep deprivation may contribute to the development of obesity through alterations in metabolic pathways and waking behavior, which includes eating behavior and physical inactivity. Research addressing these possible pathways will benefit individuals in modifying sleep to prevent and manage obesity. It is hypothesized that increasing sleep duration in obese individuals who experience chronic sleep deprivation will lead to a decreased BMI.

If weight gain is observed in individuals resulting from sleep deprivation, then interventions designed to increase the amount of sleep could potentially augment the clinical interventions of increasing physical activity and improving nutrition. These interventions addressing inadequate sleep would involve helping them modify maladaptive sleep habits in order to treat or prevent obesity.

Preliminary Research

One study subjected 12 healthy men to 2 days of sleep restriction and 2 days of sleep extension under controlled conditions of caloric intake and physical activity to determine

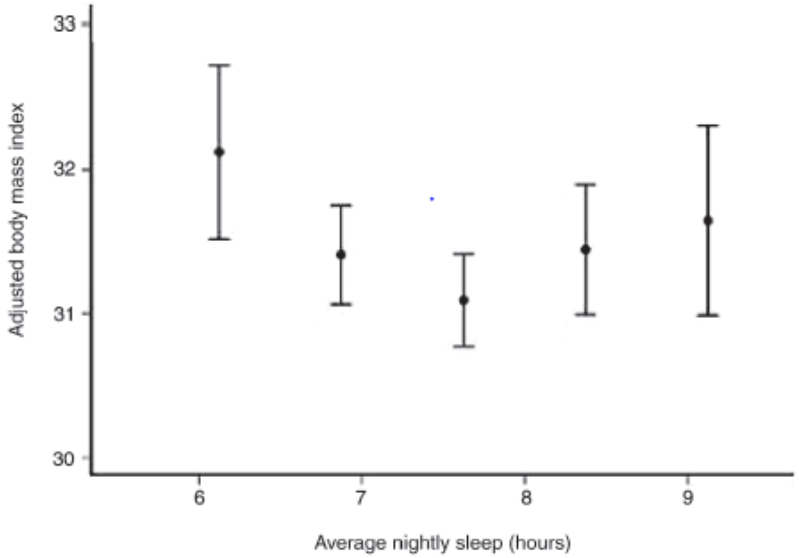
whether partial sleep curtailment alters appetite regulation (Spiegel *et a*l., 2004). It involved 2 days of 4-hour bedtimes and 2 days of 10-hour bedtimes in subjects who received a constant glucose infusion and no other source of calories (Spiegel *et al*., 2004). Caloric intake had to be kept constant to avoid meal-related fluctuations of hunger and satiety. The results showed that the participants had mean leptin levels that were 18% lower and mean ghrelin levels that were 28% higher when sleeping 4 hours than when sleeping 10 hours (Spiegel *et al*., 2004). In addition, sleep restriction was associated with a 24% increase in hunger and 23% increase in appetite, especially for high-calorie dense foods containing carbohydrates (Spiegel *et al*., 2004).



Percent difference in levels of leptin and ghrelin comparing short sleep to longer sleep conditions from two studies

A population-based study also observed an association between sleep duration, leptin, and ghrelin. The participants, 1024 volunteers from the Wisconsin Sleep Cohort Study, underwent nocturnal polysomnography (sleep test) and reported on their sleep habits through questionnaires and sleep diaries (Taheri *et al*., 2004). For individuals who slept less than 8 h, the increased BMI was proportional to decreased sleep, as is shown below (Taheri *et al*., 2004). In addition, a decrease from 8 to 5 hours of sleep was associated with a predicted 15.5% decrease in

leptin, and the same decrease of polysomnographically defined total sleep time was associated with a predicted 14.9% increase in ghrelin (Taheri *et al*., 2004). The results validate an association of decreased leptin and increased ghrelin with decreased sleep time in a large sample of adults and also in-laboratory polysomnographic data.



Curvilinear relationship between BMI and average nightly sleep
Taheri *et al*., 2004

Another epidemiologic study that showed reduced leptin levels after controlling for BMI or adiposity in habitual short-duration sleepers was the Quebec Family Study. This study aimed to explore cross-sectional associations between short sleep duration and differences in body fat indices as well as leptin levels. Compared to adults with 7 to 8 h of sleep as a reference, the adjusted odds ratio was 1.38 (95% confidence interval, 0.89 to 2.10) for those with 9 to 10 h of sleep and 1.69 (95% confidence interval, 1.15 to 2.39) for those with 5 to 6 h of sleep (Chaput *et al*., 2007). In each sex, there were lower adiposity indices in the 7- to 8-h sleeping group than in the 5- to 6-h sleeping group (Chaput *et al*., 2007).

One study examined cross-sectional and longitudinal data from a large Unites States sample to determine if sleep duration is associated with weight gain and obesity. Analysis from

the first National Health and Nutrition Examination Survey (NHANES I) indicated that among the participants between the ages of 32 and 49 years, those reporting sleeping 2-4 h, 5 h, or 6 h per night in 1982-84 had a higher mean BMI in 1982, 1987, and 1992 compared with those reporting 7 h per night in 1982-84 (Gangwisch *et al*., 2005). Additionally, getting more than 7 h of sleep per night was not significantly associated with an increase or decrease in BMI (Gangwisch *et al*., 2005).

Obesity is not just a health problem in adults, but also in children and adolescents. Some studies have been done to determine whether there is an association between short sleep duration and obesity in adolescents. In a study by Gupta *et al*., sleep duration was measured using wrist actigraphy over a 24-hour period in 383 children ages 11-16, and it was found that for every hour of lost sleep, the odds of obesity increased by 80% (2002). The findings were independent of age, gender, and race. In 2006, a cross-sectional study of 656 Taiwanese teenagers (mean age 15 years) found that the frequency of obtaining a 6-8 hour sleep duration was inversely correlated with obesity risk (Chen *et al*., 2004).

The link between sleep duration and obesity has been well established in adults, but little is known about the relationship in younger children (Lumeng *et al*., 2007). In a study in which 60 overweight children and adolescents aged 10 to 17 years were compared with matched control subjects, being overweight was associated with significantly shorter sleep duration (Beebe *et al*., 2006). Lumeng *et al*. showed that among 785 children, shorter sleep duration in 6th grade was independently associated with a greater likelihood of overweight in 6th grade, and shorter sleep duration in 3rd grade was also independently associated with overweight in 6th grade regardless of gender, race, or maternal education (Lumeng *et al*., 2007). A third study in U.S. children, which is the only study that evaluated the potential longitudinal relationship between sleep and

overweight, demonstrated that among 150 children (primarily white), shorter sleep duration between the ages of 2 and 5 years was associated with increased overweight risk at age 9.5 years (Agras *et al*., 2004).

Methods

Obesity status for all subjects is based upon BMI (weight in kilograms divided by the square of the height in meters – kg/m^2) (Gangwisch *et al*., 2005). Weight and height are measured by trained staff using a digital medical scale and stadiometer.

In studies involving sleep, scientists often use a polysomnography, or a test used to diagnose sleep disorders (MedlinePlus…2009). It consists of a simultaneous recording of multiple physiologic parameters that are related to sleep and wakefulness. Electrodes record from the scalp, eyelids, and heart using electroencephalography, electro-oculography, and chin electromyography, respectively. Like other sleep studies, a polysomnography keeps track of how often a person stops breathing for at least 10 seconds, called apnea, and how often a person's breathing is partly blocked for 10 seconds, called hypopnea (MedlinePlus…2009). The results are reported using the Apnea-Hypopnea Index (AHI), or the average number of apneas and hypopneas per hour of measured sleep, where an AHI of less than 5 is considered normal MedlinePlus…2009).

Scientists also use wrist actigraphy to approximate sleep versus wake state. Actigraphs are devices placed on the subject's wrist to record movement (Ancoli-Israel *et al*., 2003). The collected data is downloaded to a computer for analysis of activity/inactivity, which is then further analyzed to estimate wake/sleep. The technology is based on observation that there is less movement when a person is sleeping and more movement when that person is awake. Movement is sampled several times per second and stored for later analysis. Sleep/wake parameters, such as

total sleep time, total wake time, and number of awakenings, can then be derived using computer programs. Actigraphy is specifically useful in recording circadian rhythms, since it is difficult to record PSG for 24-hours and impossible to record for more than 24-hours (Ancoli-Israel *et al*., 2003). Compared to PSG, actigraphs are easier to use and less invasive.

The levels of leptin can be determined using commercially available human leptin radioimmunoassay kits (Linco Research, St. Charles, Missourri) with a sensitivity of 0.5 ng/ml, meaning 0.5 ng/ml is the lowest level of human leptin that can be detected by the assay kit. The kit uses an antibody made specifically against human leptin. In a radioimmunoassay, a specific concentration of antigen is incubated with a dilution of antiserum for binding. Then, the antibody-bound antigen is separated from the unlabeled free antigen added later on to the system, and the amount of antigen in unknown samples can be calculated with an instrument that counts radioactivity. With this kit, it is possible to determine leptin levels in serum, plasma, or tissue culture media. The levels are determined following overnight fasting. In addition to leptin levels, ghrelin levels can also be measured using radioimmunoassay (Linco Research, St. Charles, Missouri).

The proposed experiment will examine whether increasing sleep duration in obese individuals who report short sleep affects body weight through related variables such as metabolic hormones and waking behavior. It will determine the effect of sleep extension on body weight, leptin and ghrelin levels, and energy expenditure. The participants for this study will be 200 18-50 year-old obese patients who normally sleep less than 6.5 h. This age range was chosen because starting at age 60, the time it takes to fall asleep (sleep latency) increases, while total nighttime sleep decreases (Epstein, 2007). The participants will be placed in one of two groups – the Sleep Extension Group or the Comparison Group. Those in the Sleep Extension Group will

be coached to increase their sleep gradually by at least 60-90 min, possibly up to a total of 8.0 h, while the Comparison Group will be asked to continue their short sleep habits of 5 hours or less. All participants will be instructed to maintain the same diet and exercise level so as to avoid any drastic changes in weight. Those who are participating in a weight loss program will be excluded, since weight loss would not be attributed to sleep extension. In addition, patients diagnosed with sleep disorders will be excluded from the study because there is a high likelihood of the inability to increase sleep.

At the beginning of the study, baseline measurements of weight, BMI, and energy expenditure will be taken and they will be repeated at the end of the 12-month study. During the 12 months, study progress will be monitored in both groups by sleep evaluations, blood draws, and weight measurements. This will be done through 2-, 4-, 6-, 8-, and 10-month visits. At each visit, the ability of the Sleep Extension group to follow behavioral recommendations to increase sleep duration will be monitored. Sleep time will be monitored with motion sensors and self-reported sleep diaries. The Actiwatch (Mini Mitter Co., Inc. Bend, OR) is a small motion-sensing device that will be worn on the wrist to record sleep duration over a 14-day period, after which averages will be taken. Energy expenditure per day will be measured with another motion-sensing device. Actical (Mini Mitter Co., Inc., Bend, OR) will be worn on the participant's hip for the same 14 days to capture the participant's energy expenditure. Weight and BMI will also be calculated at each visit. Finally, there will be morning blood draws to measure leptin and ghrelin levels at the beginning and end of the study. At 18 months, there will be a follow-up visit, during which the same measurements will be collected from all participants and compared to those collected at the end of the 12 months.

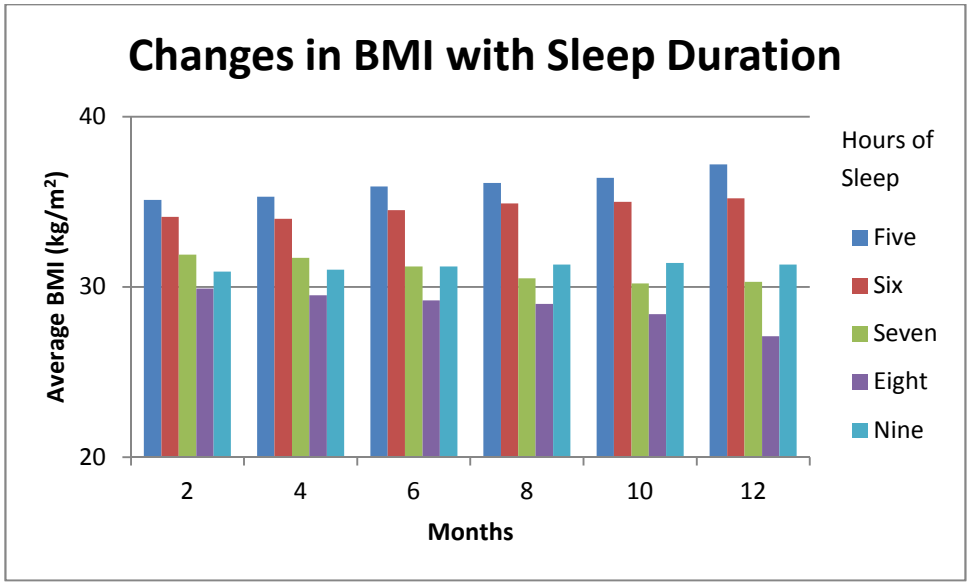
Those patients in the Sleep Extension Group will receive a 6-step sleep plan (Epstein, 2007) to increase their hours of sleep. Step 1 is to recognize the importance of sleep. Sleep is essential to a person's health and well-being. Experts believe 7.5 to 8 hours of sleep is what most people need to function at their best (Epstein, 2007). Step 2 is to adopt a healthy lifestyle by exercising regularly, maintaining a healthy diet, and avoiding cigarettes and excessive alcohol. Step 3 is to maintain good sleep habits. One of those habits is keeping a regular sleep/wake schedule, which keeps the circadian cycle synchronized because the body expects specific sleep and wake-up times. It is also useful to develop a pre-sleep routine that includes non-strenuous activity, such as reading, watching television, or listening to music, for 15-20 minutes. Other habits are to reserve the bedroom only for sleep and intimacy so that the body can associate the bed with sleep, to avoid frequent naps so as to confine sleep to one long nighttime segment, and to get out of bed if unable to fall asleep to avoid frustration.

Step 4 is to create the most adequate sleep environment to promote sleep. This step involves controlling any bedroom noise that interferes with sleep, blocking out excessive light, which signals the biological clock in the brain that it is time to wake up, and keeping the bedroom cool and ventilated. It also involves turning the alarm clock around to avoid staring at the time and making the bed comfortable, such as by changing the mattress or finding comfortable blankets and pillows. Step 5 is to be aware of beverages and substances that interfere with sleep. Caffeine, for example, boosts alertness and lengthens the time it takes to fall asleep, while alcohol decreases sleep latency (Epstein, 2007). With alcohol consumption, deep sleep (Stages 3 and 4) and REM sleep are reduced, so that most of the sleep is Stage 1 or 2, meaning the person is likely to wake up more times. Finally, step 6 is to consult a physician if

unable to extend sleep because it may be due to a sleep disorder. However, all participants will be tested for any sleep disorders.

Results

The predicted results are that the participants in the Comparison Group, who were asked to continue their habitual short sleep habits of approximately 5 hours, will experience an increase in BMI over the 12- month study period. Meanwhile, those in the Sleep Extension Group, who were asked to increase sleep duration gradually, will experience a decrease in BMI over the same period of time.



According to the graph, it is projected that there will be a decrease in BMI for those in the Sleep Extension Group, who sleep seven, eight, or nine hours. For example, the graph shows that the BMI for participants sleeping eight hours is expected to decrease from 30 to approximately 26 by the end of the 12-month period. Similarly, the BMI for participants sleeping seven hours will decrease by the end of the study. However, it is expected that sleeping eight hours, rather than seven, will have a greater effect on BMI.

For the participants in the Comparison Group, maintaining sleep at five or not longer than six hours each night will lead to an increase in BMI. The projected data on the graph shows an increase in BMI from 35 to about 38 for subjects who sleep five hours. Even though there will also be an expected increase in BMI for participants who sleep six hours each night, this increase will not be as high as the increase experienced by those who sleep only five hours.

It is predicted that sleep duration will have an effect on daytime leptin levels (ng/ml) and ghrelin levels (pg/ml). Sleeping an average of 5 hours each night will be associated with a decrease in levels of leptin and an increase in levels of ghrelin. With sleep loss, high ghrelin and low leptin levels will be associated with increased BMI. Meanwhile, sleeping an average of 8 hours each night should result in higher leptin levels and lower ghrelin levels than those observed for participants sleeping 5 hours.

Finally, participants in the Comparison Group are expected to experience an increase in food intake and a reduction in energy expenditure (kcal or METS) as validated by the Actical system. Sleep restriction will most likely be accompanied by increased consumption of energy from snacks and a preference towards carbohydrates. Participants in the sleep extension group will experience a decrease in food intake and may experience no change in physical activity or an increase in physical activity as a result of increasing sleep duration.

Discussion

People who don't sleep adequately have physiologic abnormalities, such as metabolic and endocrine alterations, that increase appetite and calorie intake (Van Cauter and Knutson, 2008). Leptin levels drop in subjects who are sleep deprived, and low leptin levels stimulate hunger and appetite (Van Cauter and Knutson, 2008). Leptin may act directly or indirectly on the CNS to inhibit food intake or even regulate energy expenditure as part of a homeostatic mechanism to

maintain the adipose mass constant (Bjørbæk and Kahn, 2004). Decreased levels of leptin due to shorter hours of sleep suggest that chronic partial sleep deprivation is one important factor causing obesity.

In the study by Spiegel *et al*. designed to determine if partial sleep deprivation alters appetite regulation, the change in the ratio of ghrelin-to-leptin between the two conditions (sleep restriction and sleep extension) was strongly correlated to the change in hunger ratings. This finding suggests that the changes observed in these appetite-regulating hormones were partially responsible for the increase in appetite and hunger. The changes in hormone levels indicate that if allowed unlimited amounts of food, the subjects would have increased their food intake. Additionally, the increase in appetite was particularly strong for nutrients with a high carbohydrate content (Spiegel *et al*., 2004), which shows that a brain that has been sleep-deprived craves its primary fuel, glucose.

The findings from the Wisconsin Cohort Study showed that less sleep from a mean of 7.7 hours was associated with a dose-dependent increase in BMI, but that sleep time of more than those hours was also associated with increased BMI (Taheri *et al*., 2004). However, it was the lack rather than the excess of sleep time that affected body weight in greater proportions. The findings also support the hypothesis that sleep loss alters the ability of leptin and ghrelin to accurately signal caloric need, acting together to produce an internal perception of insufficient energy availability. Their findings are strengthened by the large and well-characterized population-based sample, attention to bias and confounding factors, such as BMI, age, and sex, as well as in-laboratory polysomnographic data. The observed hormonal changes (decreased leptin and increased ghrelin) with partial sleep deprivation were consistent and of significant magnitude because they were associated with increased BMI (Taheri *et al*., 2004). Thus, they

play a contributory role in the development of overweight and obesity with sleep deprivation. Most importantly, the study represents the first demonstration of a correlation between hormone levels and both self-reported (sleep questionnaires and diaries) and polysomnographically-determined sleep.

The study by Gangwisch *et al*. that sought to determine if sleep duration is associated with obesity and weight gain found significant differences in sleep duration by obesity status only for subjects who were between the ages of 32 and 49 years at baseline (2005). Different relationships found between sleep duration and obesity in the younger and older age groups could have been due to age-related sleep changes. For example, advanced age is associated with changes in sleep characteristics and structure, specifically with increased difficulties in sleep initiation and maintenance (Webb, 1989). In addition, the younger and older groups lived through different historical time periods with different stressors and health practices, such as physical activity and diet. There was not a U-shaped relationship between BMI and sleep duration. However, among those with sleep durations of less than 7 hours, as their sleep durations decreased, their likelihood of being obese progressively increased (Gangwisch *et al*., 2005), indicating that there is a strong link between sleep duration and weight gain.

The study by Gupta *et al*. used an objective measure of sleep habits (actigraphy) to determine the relationship between sleep duration and weight in adolescents (2002). It was found that for every hour of lost sleep, the odds of obesity increased by 80% (Gupta *et al*., 2002). While the study results could not establish sleep debt as a causative factor in obesity, it did show that the likelihood of obesity in individuals with few hours of sleep is significantly greater than in individuals who sleep longer. Because the study covered only one 24-hour period in an adolescent's life, it did not allow for the most accurate representation of daily sleep habits. A

longer study would confirm or deny the association between inadequate sleep and obesity. Even so, the association of sleep time with obesity in this study was statistically significant and was observed in both male and female adolescents in a model that included various confounding factors, such as ethnicity (Gupta *et al*., 2002). Short sleep duration may affect adolescents more than it affects adults. Adolescence is a critical development period in which sleep deprivation commonly occurs due to changes in the biological timing of sleep (Carskadon *et al*., 2004). These changes include going to sleep at later times and reducing the amount of sleep adolescents get because they must wake up early for school (Carskadon *et al*., 2004).

In a study examining the relationship between amount of sleep and health in adolescents, one key finding is that adequate sleep, defined as 6-8 hours per night regularly, is positively associated with health status and health-related behaviors (Chen *et al*., 2006). Adolescents who frequently obtained 6-8 hours of sleep each night had a reduced probability of becoming overweight (Chen *et al*., 2006). The study used subjective self-reporting of sleeping hours to determine adequate sleep time, which could have caused significant measurement errors. Further research should use more objective measures, such as actigraphy to measure sleep time. Additionally, the data was obtained from only one county in Taiwan. However, the consistent findings from this investigation in another continent suggest that associations between short sleep duration and overweight are independent of ethnicity.

Collectively, the studies done on children provide evidence for an association between shorter sleep duration and an increase in the likelihood of obesity. The study by Beebe *et al*. used both objective (actigraphic and polysomnographic) and subjective (parent- and self-report questionnaire) sleep assessment methods (2006). The data also supports the research literature that links short sleep to excessive weight gain (Agras *et al*., 2004). Agras *et al*. showed a

negative correlation (-0.21) between hours of sleep and overweight (2004). The length of the children's sleep was assessed by annual parent report at ages 2 through 5, and this measure was stable from 3 to 5 years, making the data appropriate for the study.

Lumeng *et al*. was the first study to examine the association between short sleep duration and overweight risk in a relatively large U.S. cohort (2007). The findings in Lumeng *et al*. that shorter sleep duration in 3rd grade is independently associated with a greater likelihood of overweight in 6th grade (2007) suggest that one preventive approach to being overweight may be to ensure adequate sleep in childhood. Since the protective effect of longer sleep duration in the study was mediated by sleep onset rather than wake times, the best recommendation would be for parents to enforce an age-appropriate bedtime. The current research cannot yet support the assertion that longer sleep will contribute to weight loss, but successful interventions for sleep problems have been associated with gains in academic, behavioral, and emotional functioning (Gozal, 1998).

The findings from two studies, Spiegel *et al*., 2004 and Taheri *et al*., 2004, suggest that short-term sleep restriction alters metabolic hormones under controlled laboratory conditions in a manner that is consistent with weight gain and obesity. However, it is not clear whether the physiological effects of chronic partial sleep deprivation under laboratory conditions and for a period of a few days are equivalent to the effects in free-living individuals (Magee *et al*., 2009). It can be assumed that there is some degree of physiological adaptation to the effects of sleep deprivation, even though the extent and nature of such adaptation is not well known (Magee *et al*., 2009). Additionally, the causes of sleep deprivation could differ considerably between individuals and the impact of sleep deprivation on energy balance may depend on its specific cause.

One of the limitations of the studies reviewed may be that part of the evidence comes from short-lived severe sleep deprivation experiments that cannot be translated to long term effects in the population (Cappucio *et al*., 2008). Laboratory studies of sleep restriction cannot be conducted for periods of time that are longer than 1 to 2 weeks (Knutson and Van Cauter, 2008). Second, studies have used sleep questionnaires to determine self-reported sleep duration, and there is the possibility that participants provided an inaccurate number of hours. Even so, in one study, self-reported sleep duration was validated against actigraphy (Lockley *et al*., 1999). Because good agreement has been found between self-reported sleep durations and those obtained through actigraphic monitoring, both methods can be used in sleep studies.

It is important to consider that the association between chronic sleep deprivation and obesity may be bidirectional. Even though there is evidence indicating that chronic sleep deprivation contributes to obesity, it is also possible that obesity and its associated changes affect sleep adversely, leading to the development of a vicious cycle. Obesity increases the risk of medical conditions, such as osteoarthritis, gastroesophageal reflux, asthma, and heart failure that can disrupt sleep and even lead to insomnia (Hu and Patel, 2008). However, whether or not obesity has an effect on sleep, independent of its medical complications, is unclear. Most of the data suggests that the effect is in the opposite direction. The positive findings from 4 studies (Spiegel *et al*., 2004; Taheri *et al*., 2004; Chaput *et al*., 2007; Gangwisch *et al*., 2005) support the hypothesis that short sleep duration causes weight gain rather than vice versa. Still, there is a need for more research to understand the magnitude of the effect of sleep deprivation on obesity.

There are many potential mechanisms through which short sleep duration may result in obesity. Short sleep duration affects both energy intake and energy expenditure. Since the interaction between short sleep duration and obesity is complex, there are multiple inter-related

factors operating downstream of sleep duration that combine to result in obesity. First, chronic sleep deprivation results in changes in the levels of several hormones, such as leptin and ghrelin (Taheri *et al*., 2004; Spiegel *et al*., 2004). The hormonal changes contribute to increased hunger and appetite and a preference for calorie-dense food (Spiegel *et al*., 2004). Chronic sleep deprivation also affects waking behavior and specifically, promotes patterns of behavior that cause weight gain. According to results from the National Sleep Foundation's "Sleep in America" Poll, not getting enough sleep was associated with irritability, impatience, pessimism, and feeling stressed (2002). These feelings and emotional states could then function to lessen an individual's willpower to follow a diet or exercise routine, and consumption of food with a high-energy content and sedentary behavior are well known risk factors for obesity (Hill *et al*., 2003).

Those who get insufficient sleep are more likely to experience fatigue and excessive daytime sleepiness (Durmer and Dinges, 2005). This could lead them to engage in behaviors such as consumption of high-energy drinks or food to counter the effects of fatigue. Fatigue may also contribute to reduced daytime physical activity and increased sedentary activities like television viewing. When energy intake exceeds expenditure over a prolonged period of time, there is a potential to affect the processes that regulate body weight, leading to obesity over time (Spiegelman and Flier, 2001). Additionally, the extra time awake provides individuals with an increased opportunity to eat. They increase their calorie consumption by snacking during the night when they would normally be sleeping.

The profile of hormonal changes suggests that one pathway linking chronic sleep deprivation to obesity involves metabolic hormones. Leptin, which is released in proportion to adipose tissue amount, acts on hypothalamic circuits to reduce energy intake and increase energy expenditure (Porte *et al*., 2002). Therefore, the reductions in leptin observed with sleep

restriction indicate increased food intake and reduced energy expenditure. Meanwhile, ghrelin is released primarily from the stomach when nutrient levels are low and it acts on the hypothalamic pathways to stimulate food intake (Wren *et al*., 2001). Thus, the elevations in ghrelin also observed with sleep restriction indicate increased food intake.

Due to the level of causal evidence, increasing sleep duration would serve as a strategy to decrease obesity. While obesity is reversible, voluntary weight loss is difficult to achieve and maintain. Therefore, preventing some fraction of obesity prevalence through changing sleep duration would benefit population health. It is not possible for an individual to sleep away their obesity, but if short sleepers increase their sleep time, the population as a whole will be healthier and rank lower in mean BMI.

Manipulating sleep time duration in the proposed study would demonstrate whether changing the risk factor will lower the risk for overweight and obesity. Subjects in the Sleep Extension Group would have a decreased BMI due to increasing sleep time, while subjects in the Comparison Group would have an increased BMI due to lack of adequate sleep. Since sleep duration is known to influence hormone levels (Spiegel et al., 2004; Taheri *et al*., 2004), food intake (Nedeltcheva *et al*., 2009), and energy expenditure (Schmid *et al*., 2009), the effects of partial sleep deprivation in subjects in the Comparison Group would include low leptin and high ghrelin levels, increased food intake and weight gain, and possibly decreased physical activity. However, increasing sleep in subjects in the Sleep Extension Group would lead to normal hormone levels, decreased food intake, and weight loss, leading to a lower BMI. There may also be an increase in physical activity.

One of the challenges for the proposed study design is that self-reported sleep duration is at best imprecise. In addition, the mode of monitoring sleep will be indirect through the use of

motion sensors (Actiwatch) that determine the likelihood of wake and sleep at any given time during monitoring. However, the technology is accurate, and self-reported sleep will help clarify unusual periods of inactivity. It may also be difficult to obtain accurate measurements of food intake in free-living individuals. Obese individuals tend to underreport food intake by as much as 30% (Lichtman *et al*., 1992), and they are thought to ingest more calories than individuals who are not obese. Also, it is possible that some subjects may show a strong propensity to overeat and gain weight irrespective of the presence or absence of sleep loss. The effects of sleep deprivation may have more negative metabolic consequences in persons with such preexisting susceptibility.

Another challenge is that behavioral interventions are difficult to implement, especially in outpatient settings. Not all participants may go to bed at a consistent time each night and get up at a similar time, or they may not avoid taking excessive worries to bed, making it difficult to sleep. In addition, studies about obesity require a large sample size and long duration, and it may be difficult to recruit all of the participants needed into the study. Participants have to be told what kind of testing will be done and to which group they will be assigned. This could lead them to withdraw or decide not to comply with the protocols. The 12-month design is meant give participants sufficient time for them to make lifestyle changes, and it accounts for seasonal changes that may affect sleep or eating. However, the 18-month follow-up visit may have to be extended for additional data from longer study duration.

It is necessary for future research investigating the link between chronic partial sleep deprivation and obesity to address the underlying causes of partial sleep deprivation. The causes or determinants of partial sleep deprivation have been largely overlooked. These causes need to be examined because the relationship between partial sleep deprivation and obesity may depend

on a specific cause. Even the potential to modify sleep duration to help prevent or manage obesity may depend on the specific factor contributing to partial sleep deprivation

Many questions still have to be answered to determine causality. Prospective studies in which weight, height, waist measurements and adiposity are measured at baseline and again at subsequent data collection times are needed, as well as more accurate objective measurements of sleep duration (including naps) and confounding factors, such as family history, depression, and demographic factors. Finally, controlled trials are needed to assess the potential for sleep-promoting interventions to combat the obesity epidemic.

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Conclusion

Partial chronic sleep deprivation is an increasingly prevalent behavior in modern society that may increase the risk of weight gain and play a role in the current epidemic of obesity. Sleep deprivation has been shown to contribute to the obesity epidemic by altering neuroendocrine hormones, including leptin and ghrelin levels (Taheri et al., 2004; Spiegel et al., 2004), and affecting waking behavior, specifically food intake (Nedeltcheva et al., 2009) and energy expenditure (Schmid *et al*., 2009). Because sleep duration is a potentially modifiable risk factor, increasing sleep may have important clinical implications for the prevention and treatment of obesity. The results from the proposed study will demonstrate whether increased sleep duration is associated with a decreased BMI and obesity risk. Furthermore, additional studies conducted in real-life conditions over long periods of follow-up with an accurate monitoring of sleep duration and energy balance will be necessary to better understand the effect of adequate sleep in fighting against obesity. Ensuring adequate sleep may have other added health and educational benefits. Thus, efforts to educate the public regarding the deleterious effects of partial sleep deprivation on long-term health and well-being should start in early life.

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