THE IMPROVEMENT IN OBSTRUCTIVE SLEEP APNEA AND SLEEP DURATION AND ITS ASSOCIATION WITH CHANGES IN MACRONUTRIENT INTAKE IN ADULTS

A Thesis

Presented to

The Graduate Faculty of The University of Akron

In Partial Fulfillment

of the Requirements for the Degree

Master of Science

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August, 2010
THE IMPROVEMENT IN OBSTRUCTIVE SLEEP APNEA AND SLEEP
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Thesis

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Background: Obstructive Sleep Apnea (OSA) is prevalent in three to seven percent of American adults, and the diagnostic criterion is the Apnea-Hypopnea Index (AHI). While obesity is a major cause of OSA, various researchers have reported significant associations between moderate to severe OSA, sleep curtailment and increased caloric intake. Also, when energy intake exceeds output over time it results in obesity, a public health problem associated with other diseases.

Purpose: The study aimed to find a significant relationship between improvement in OSA with change in total energy intake and also a change in the proportion of energy as percent fat, carbohydrate and protein. If energy intake decreased, it will then be accompanied with some weight loss overtime to help control OSA related obesity.

Methods: Fifty-three subjects with moderate to severe OSA (AHI≥15) were recruited from an existing data set available from the study ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome’ conducted from 2003 to 2007 at the Dahms Clinical Research Unit in Cleveland, Ohio. Access to data was made available by the principal investigator, Dr. Susan Redline. Dietary information from a 24-hour recall was entered into Nutrition Data Systems for Research (NDSR) software and analyzed with Microsoft Excel and JMP statistical tools by the researcher.
Results: As OSA improved there was a significant increase in the percentage of total kilocalories (kcal) consumed as fat (p=0.046). Conversely, the percentage of total kcal consumed as carbohydrate and protein did not change with improvement in OSA.

Conclusion: Dietary intakes of total energy, carbohydrate and protein were not significantly different after improvement in OSA after Continuous Positive Airway Pressure (CPAP). However, improvement in OSA was associated with an increase in the percentage of kcal consumed as fat. Considering the limitations associated with the use of a 24-hour recall, this area of research needs additional study with multiple dietary collection and energy expenditure methodology and determination. Perhaps additional thorough dietary analyses would more clearly demonstrate the alterations and trends in macronutrient intakes with OSA improvement.
DEDICATION

I dedicate this work to the Lord God Almighty of the whole earth whom by his might and power I have been able to complete this work. I can do all things through Jesus Christ who strengthens me.
ACKNOWLEDGEMENTS

I thank the Lord God Almighty through his son Jesus Christ for the strength he provided throughout my work. I am grateful to my advisor Dr. Marino for her unfailing commitment to see the completion of this work. My gratitude goes to Dr. Steiner and Dr. Hudak for taking time off their busy schedules to ensure the accuracy of this research. I acknowledge Dr. Susan Redline, Joan Aylor and Alicia Thomas for their patience and the opportunity to be a part of this important study.

I thank my parents, sister and brothers for their concern and prayers throughout the time I had to complete this work. I thank my husband for forbearance, understanding and all the resources he put into this work.
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CHAPTER I
THE PROBLEM

Introduction

The quality of sleep and nutrition are essential, natural and unavoidable aspects of the well-being and good health of all living things. Since the 1970s physicians have begun to recognize many of the detrimental consequences of sleep disturbances produced by a group of disorders characterized by abnormalities of respiratory pattern (pauses in breathing) or the quantity of ventilation during sleep (1). These disorders known as Sleep Disordered Breathing (SDB) have been recognized since the fourth century BC (2). Cross sectional studies indicate that (SDB) currently affects two to four percent of middle aged populations worldwide and occurs commonly in individuals with diabetes, hypertension, and obesity (3).

The most common type of SDB is Obstructive Sleep Apnea (OSA), the recurrent partial or complete collapse of the upper airway during sleep. It is characterized by stops in breathing during sleep, usually for ten seconds or longer, and may be accompanied by snoring. This causes the amount of oxygen in the blood to drop and alert the brain to cause awakening which results in daytime sleepiness (4). The prevalence of OSA is estimated to be three to seven percent with certain subgroups of the population bearing higher risk (2).
The current standard for diagnosis of all SDB is by polysomnography (PSG) and the diagnostic criteria for OSA include Apnea-hypopnea Index (AHI) which is the average number of apneas and hypopneas per hour during sleep. The suggested AHI threshold is five, 15 and 30 events per hour for mild, moderate and severe OSA (5). The annual cost related to the diagnosis and treatment of severe SDB in the United States is estimated to be at least three million dollars. Much higher costs are projected for treatment of the larger number of individuals with milder disease and associated co-morbidity (6).

Short sleep duration as a consequence of OSA has been associated with increased prevalence of obesity in Spain, Japan and the United States (7). It is estimated that sleep curtailment occurs in moderate to severe OSA in approximately nine and four percent of middle aged men and women respectively. In addition, a study reported sleep restriction is significantly associated with increased hunger (p<0.01) (8).

Various studies have concluded that the major risk factors of OSA are obesity, gender, genetics, age and hormonal factors as well as other causal factors like structural abnormality in the face, skull or airway passages (2). These factors interact in a multifaceted manner in the pathogenesis of SDB. In addition, the connection between OSA and obesity is very complex and likely represents an interaction of biological, nutritional and lifestyle factors.

It is well known that when energy intake exceeds output, weight gain and eventually obesity will result. However, if obesity results in SDB and dietary overconsumption results in obesity, it is possible that individuals with SDB have increased dietary intake relative to their need. Although the interrelationship between
nutrient intake and sleep duration has been studied, there is a paucity of research investigating the association between sleep duration and macronutrient intake in individuals with OSA. However, some studies have reported that a low caloric diet improves OSA.

Existing cross-sectional studies suggest that an association between short sleep and obesity may be accompanied by changes in concentrations of the orexigenic hormone ghrelin and anorexigenic hormone leptin which are important in appetite regulation (9). Sleep deprivation, also an end result of OSA, causes decreased leptin and increased ghrelin which may promote an increase in appetite and impact dietary intake. Also, it is hypothesized that disturbance in sleep causes weight gain by limiting physical activity, and also may influence food choices thereby affecting energy balance related to consumption of carbohydrate, proteins and fat (10). Among all articles searched and reviewed no study has compared dietary changes in subjects at baseline and after they were treated with continuous positive airway pressure (CPAP).

The aim of this study was to investigate the association between macronutrient intakes and sleep duration in individuals with OSA, using existing data, and to determine whether the severity of sleep duration or sleep apnea correlates with change in macronutrient intake. Data were obtained from clinical trial study on ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome’ sponsored by Dietrich Diabetes Research Institute (DDRI). A 24-hour recall used to collect dietary information was entered into Nutrition Data System for Research (NDSR) 2007 software.
Purpose of the Study

Sleep restriction could affect exogenous factors such as food choice, and time available to eat, both important in energy balance. It is known that amount of energy intake directly affects body weight. Body weight is directly proportional to the amount of food intake relative to need; and an increase in body weight may lead to obesity.

Hence, using baseline data, the purpose of the study was to determine the relationship between macronutrient intakes and sleep duration in individuals with OSA. In addition, this study investigated whether improvement in sleep duration or sleep apnea severity correlate with change in macronutrient intake. Sleep affects various physiological processes in our body and will change specific hormones that regulate appetite and hunger as well as influence energy expenditure. The relationship among the different factors that affect sleep duration in OSA is a cyclic one which may include the alteration in normal dietary intake.

Significance of the Study

Obesity, appetite, hormonal changes, metabolic rate and most importantly nutrition are related to sleep apnea and OSA. Currently, obesity is a public health burden in the United States and a risk factor for many other diseases including OSA (11). A number of studies show a direct relationship between obesity and OSA (12, 13, 14, 15). Based on this finding, it is valuable to investigate the relationship between food intake (macronutrient) and OSA since obesity is related to the amount and kind of energy consumed.
Knowledge about the amount and proportion of macronutrients consumed by OSA individuals may contribute to existing recommendations to prevent OSA related obesity. From a nutrition perspective, it may be helpful to understand the relationship between energy consumption alterations and OSA occurrence and amelioration.

Hypotheses

1. Improvement in OSA is correlated with a change in total energy intake.

2. Improvement in OSA is correlated with a change in the proportion of total energy consumed as fat, protein and carbohydrate.

Assumptions

This research will be based on some assumptions. First, the data available for this study were assumed to be accurate because the original study protocol described data collection as standard. The most current instruments were used for all measurements for the duration of the study. No error or problem with instrumentation was reported. The time frames proposed for the study were successful and participants complied with directions, participation and treatment plans.

The data from the study were double-blinded, hence bias in data collection was reduced. Each subject was only unblinded after his or her participation was completed. Also, only the dedicated research sleep technician who was responsible for initial Continuous Positive Airway Pressure (CPAP) education and performing polysomnography (PSG) was unblinded.
Accuracy of data entry were determined by a quality control specialist after the manual input of all dietary information on the 24-hour recall for each individual subject for baseline and after CPAP treatment.
Sleep Disordered Breathing (SDB)

Sleep cannot be avoided by anyone living thus humans spend approximately 30% of their lives sleeping because of its necessity for our health (1). Sleep Disordered Breathing (SDB) is a group of disorders characterized by abnormalities of respiratory pattern on the quantity of ventilation during sleep (11). Many clinicians regard SDB as a spectrum of diseases comprising sleep apnea, the cessation of airflow for at least ten seconds usually accompanied by snoring which is also subdivided into obstructive, central, and mixed sleep apneas (16).

Obstructive Sleep Apnea (OSA) also known as Obstructive Sleep Apnea Syndrome (OSAS) is the most common type of abnormal respiratory pattern during sleep (16). Apnea means gap in breathing and is defined as cessation of airflow for at least 10 seconds using a valid measure of airflow such as polysomnography (PSG).

In OSA, the reduction of airflow leads to alterations in gas exchange and recurrent arousals from sleep. This consequently affects nocturnal sleep quality and results in daytime fatigue and sleepiness which can lead to various health consequences such as impaired cognitive function, work performance, and quality of life, if left untreated. Research suggests that OSA may contribute as an independent risk factor for several
clinical consequences, including systematic hypertension, cardiovascular disease, stroke, and abnormal glucose metabolism (2).

In a review by the American Academy of Sleep Medicine (AASM), the evolution of technological means of measuring airflow and other respiratory parameters combined with changing understanding of the pathophysiology of sleep related breathing disorders (SRBDs) has resulted in various definitions of apneas and respiratory effort related arousals (RERAs). The severity of sleep apnea is typically assessed with the apnea–hypopnea index (AHI); the number of apneas and hypopneas per hour of documented sleep (2, 17). Mild sleep apnea has been defined as an AHI of 5 to 15 events per hour, moderate sleep apnea defined as 15 to 30 events per hour, and severe as an AHI more than 30 events per hour (17).

The most common sleep recording used to diagnose sleep apnea also known as the “gold standard” diagnostic test for OSA is the polysomnogram. This diagnosis is defined on the basis of symptoms of day time sleepiness and objective measures of disordered breathing during sleep (3). The test records brain activity, eye movement, muscle activity, breathing, heart rate and percentage of oxygen in the blood while sleeping. Treatment and diagnosis have remained largely unchanged over the past 25 years despite increasing awareness of the condition and improved diagnostic procedures (3).

In moderate-to-severe OSA/hypopnea syndrome, treatment with continuous positive airway pressure (CPAP) has proven to be effective (3). CPAP is the most common treatment for sleep apnea which involves wearing mask over your nose during
sleep (18). However, CPAP remains somewhat cumbersome and hence not associated with optimum compliance rates.

Epidemiology of Obstructive Sleep Apnea

Sleep apnea has been recognized since the 4th century BC with numerous reports throughout the 19th and early 20th century. Research on OSA, however, is relatively recent. Consequently, estimates of disease prevalence did not exist worldwide despite its increasing recognition until 15 years ago (2).

Epidemiological studies have revealed a prevalence of sleep-disordered breathing in the community of up to 20% (2). The fact that prevalence estimates of OSA from North America, Europe, Australia, and Asia are not substantially different suggests that this disease is common in developed as well as developing countries. One in 25 adult Americans (four percent) are diagnosed with OSA and it is most prevalent among certain population subsets, including those who are overweight or obese, minority race, and older (18). Despite the high prevalence in general populations and regardless of clinical and scientific advancements of OSA in the last two decades, a majority of people with this disorder are left undiagnosed (2,18).

It is of interest to note that over the past 40 years sleep duration in the United States has decreased by one to two hours. Statistical reports state that 35% of Americans reported at least eight hours of sleep in 1998, but only 26% did so in the year 2005 (19, 20).
Causes of Sleep Disordered Breathing

SDB is a complex, chronic disease, influenced by a number of causes that interact to increase the propensity for repetitive upper airway collapse occurring with sleep. Any structural abnormality in the face, skull, mouth, esophagus or airways that causes some obstruction or collapse in the upper airways and reduces air pressure can produce sleep apnea syndrome. Enlarged soft palates are also associated with many cases of sleep apnea.

Excess Body Weight

Among the known causes of sleep apnea, the one of primary relevance is obesity. About 40% of OSA cases are found among patients with morbid obesity (15). The effect of obesity on sleep apnea susceptibility is related to the distribution of adiposity between the central and peripheral compartments such that visceral fat accumulation and large neck circumference are predictive factors for OSA. Central obesity accounts for the strong male predominance of this disorder, whereas peripheral adiposity may protect women from developing sleep apnea. Obesity and particularly central adiposity can increase sleep apnea susceptibility by increasing upper airway mechanical loads and/or decreasing compensatory neuromuscular responses (21).

Risk Factors for Sleep Disordered Breathing

Several risk factors include obesity, age, sex, heritable factors among others. Male sex is a strong risk factor and confers a two to three fold increased risk of sleep apnea in the population. This may be related to the differences in distribution of adipose tissue in
men who exhibit a predominately central fat deposition pattern around the neck, trunk, and abdominal viscera as compared with women.

The prevalence of OSA associated with accompanying daytime sleepiness is approximately three to seven percent for adult men and two to five percent (2) for adult women between ages 30-60 (16) in the general population. However, sleep apnea may be under-diagnosed in women, particularly older women. Older women have a similar incidence of sleep apnea as men their own age (16).

In a retrospective study of 160 adult male patients who snored and were diagnosed with OSA, primary snoring and mild OSA directly correlate with BMI. The subjects with moderate to severe OSA had no significant increase in BMI. The results from this study then suggested because of an insignificant change in AHI in the subjects with severe OSA, the progression of OSA is mainly dependent on weight gain as compared to how long an individual has OSA (22).

There is an interaction between race and sleep apnea. Compared to Caucasian, African-Americans face a higher risk for sleep apnea. This is because of high rate of obesity reported from various studies in this group. Pacific Islanders and Mexicans also face the risk of sleep apnea but not as much as African-Americans.

To examine the relationship among obesity, sex, and age and passive upper airway properties in a large cohort study of 56 normal subjects and 108 sleep apnea patients assessed by determining the pharyngeal critical pressure under hypotonic conditions (Pcrit), Passive Perit was markedly elevated in men compared with women independent of disease or obesity. This demonstrated that the increase in passive Pcrit with obesity was greater in men than women. Passive Pcrit is suggested to be
differentially controlled by sex, age and BMI, and that its alterations partly mediate the relationship between these sleep apnea risk factors and OSA. The finding suggests age, sex and obesity are major risk factors of sleep apnea (12).

Medical Consequences of Sleep Disordered Breathing

In addition to sleepiness and daytime performance deficits, growing data indicate that SDB is a risk factor for hypertension, cardiovascular disease, stroke, mortality and obesity. Obesity is also strongly associated with comorbidities such as type 2 diabetes mellitus, hypertension, heart disease, gall bladder disease, and sleep apnea.

The strongest data are from the Sleep Heart Health Study (SHHS), a large, prospective study of SDB and Cardiovascular disease. Although the prospective analyses are not yet available, the cross-sectional data indicate that modest levels of SDB increase risk of hypertension by 40-70% (23) and of cardiovascular disease by 30-40% (24). Also, longitudinal data from the Wisconsin Sleep Cohort indicate that baseline SDB (AHI>15) increases risk of incident hypertension by greater than two fold over eight years (25).

A cross-sectional study of patients with a definite diagnosis of obstructive sleep apnea syndrome (OSAS) was performed using new diagnostic criteria for metabolic syndrome that were designed for the Japanese population. The prevalence of metabolic syndrome in patients with OSAS referred to a medical center was investigated. Clinical features and comorbidities related to metabolic syndrome were compared between 819 patients with OSAS (719 men and 100 women) and 89 control subjects without OSAS. Results indicate that metabolic syndrome was significantly more common in the patients with OSAS than in the controls. Generally, both sexes with OSAS had a higher risk of
metabolic syndrome compared with controls. However, the risk was significantly higher in women with severe OSAS (AHI \( \geq 30 \) h). Risk factors for metabolic syndrome differed by gender. In men, age, body mass index (BMI), and OSAS (AHI \( \geq 15 \) h) were significantly associated with metabolic syndrome, whereas, in women, BMI was the only risk factor for metabolic syndrome. The increase of metabolic syndrome in Japanese OSAS patients suggests that this patient population is burdened with multiple risk factors for cardiovascular disease (26).

OSA is associated with vascular risk factors and with substantial cardiovascular disease morbidity and mortality. In an observational cohort study, OSA retained a statistically significant association with stroke and death. The OSAS significantly increases the risk of stroke and death from any cause, and the increase is independent of other risk factors including hypertension (27). According to a prospective study sleep apnea was significantly associated with the risk of stroke among patients with coronary artery disease who were evaluated for coronary intervention. The result indicated that out of the 392 patients, stroke occurred in 12%, six were hemorrhagic strokes and 41 were infarctions. However, death and acute myocardial infarction were not associated with sleep apnea among the present patients (28).

In the Wisconsin sleep cohort, a population based longitudinal study of sleep disorders investigated the less understood relationship between SDB and diabetes mellitus. Self-reported diabetes was three or four times more prevalent in subjects with an AHI of 15 compared to with those who had an AHI of less than five. Although the data do not provide evidence for a causal link between these two conditions, the findings from the study have clinical relevance. The strong association of SDB with diabetes supports
the need for a lower threshold for sleep evaluation referral in patients with diabetes and vigilance in those taking care of patients with SDB to consider the possibility of concurrent diabetes. Furthermore, treatment of sleep apnea improves insulin sensitivity and could benefit the metabolic profiles of these patients, although the benefit is not well defined. Thus, treatment of SDB in patients with diabetes may still be beneficial, whether SDB has an indirect or a direct role (29).

Sleep and Energy Balance

Some literature states that the effect of the obstructive sleep apnea syndrome on energy expenditure is controversial. Twenty-four apneic men took part in a cross-sectional study and were classified in quartiles of nocturnal desaturation severity to assess the relationship between 24-hr energy expenditure or sleeping metabolic rate and features of the obstructive sleep apnea. Whole body indirect calorimetry (respiratory chamber) and hydrodensitometry were used to measure 24-hr energy expenditure, sleeping metabolic rate and body composition. The results showed that 24-hr energy expenditure and sleeping metabolic rate were similar among quartiles. However, when expressed on a per kilogram body weight basis (kcal/kg), these variables were negatively correlated with the catecholamine concentration and percentage recording time in the whole group. The authors concluded that in apneic men energy expenditure relative to body weight decreases with increasing severity of oxygen desaturation which could favor a positive energy balance (30).
Hormonal Influence

Ghrelin (orexins), a hypothalamic excitatory neuropeptide, has potent wake promoting effects. Ghrelin will also stimulate food intake under certain conditions and has provided the molecular basis for the interaction between regulation of feeding and sleeping. On the other hand, leptin (an anorexin) is a circulating hormone produced by adipocytes whose plasma levels are increased in obese and OSA individuals. Its release is inhibited by sympathetic nervous system activity. The possibility that sleep restriction may result in decreased levels of leptin may be attributed to an alterations of sympathetic outflow.

The high prevalence of OSA in obese humans and the established role of leptin as a respiratory stimulant and appetite suppressant in the mouse was the basis to test whether changes in circulating leptin and ghrelin levels were found in patients with OSA. The results indicate that serum leptin levels were significantly higher in OSA patients compared to the control group. There was no significant difference in serum ghrelin in both groups. In conclusion, elevated serum leptin levels in OSAS patients may be considered as a marker of OSA. Although serum ghrelin was significantly associated with OSAS it was also associated with BMI (31).

It has been suggested that the abnormal leptin levels are related to abnormal sympathetic activity that characterize OSA but the potential confounding effect of obesity has not been formally excluded. The independent contribution of sleep apnea and obesity to plasma levels of neuropeptide Y (NPY) and leptin was investigated in a different study (32). Their concentration was compared in 23 obese (BMI>30 kg/m2) and 24 non-obese (BMI<27kg/m2) men with OSAS, and in 19 obese and 18 non-obese men without OSAS
as control subjects. NPY levels were higher in OSA subjects independent of weight status. Leptin levels were also higher in obese subjects irrespective of presence of sleep apnea. CPAP treatment decreased NPY levels both in obese and non-obese patients whereas the leptin level decreased only in non-obese patients (32). Secondly, the plasma concentration of leptin is increased in OSA. The results contribute to better delineation of the independent effects of OSA and obesity on two peptides involved in the regulation of body weight, energy balance, and sympathetic tone (32).

Additionally, to test the hypothesis that circulating levels of leptin are influenced by sleep duration, 24 hour hormonal and glucose profiles were sampled at frequent intervals. The sympathovagal balance was estimated from heart rate variability in 11 subjects studied after six days of four hour and six days of 12 hour bedtimes, respectively (19). With the controlled caloric intake activity, leptin levels were decreased during sleep restriction compared with sleep extension. The authors found that short sleep duration in young, healthy men is associated with decreased leptin levels, increased ghrelin levels, and increased hunger and appetite (19). This hormone modulates a major component of the neuroendocrine control of appetite.

The loss of leptin signaling causes obesity in humans. Circulating leptin concentrations have a strong and positive correlation with BMI. Leptin acts to reduce food intake, increase energy expenditure, and modulate immune and inflammatory response. The nocturnal rise of leptin is partly a response to daytime meal ingestion which regulates fat mass by stimulating a decrease in food intake and an increase in energy expenditure (31, 33).
Insulin and leptin share many properties as adiposity signals. Both reduce food intake and bodyweight in a dose-dependent manner when administered directly into the central nervous system (34). Figure 2.1 shows the link between the periphery and the brain: endocrine and neuronal interaction in the regulation of energy homeostasis and appetite (34).

Figure 2.1. Endocrine and neuronal interaction in the regulation of energy homeostasis and appetite.
Sleep Duration and Energy Balance

Current research has linked reduced sleep with excess weight (9, 31, 33). Epidemiologic data indicate that self-reported sleep of less than six hours per night is associated with increased adiposity (9). Likewise, some prospective studies in adults have linked short sleep duration with greater risk of weight gain and obesity (9). A study that measured energy intake and expenditure of 11 voluntary sedentary men and women between 34 to 49 years suggest recurrent bedtime restriction can modify the amount, composition and distribution of human food intake, and reduced sleep in an obesity promoting environment may facilitate excessive consumption of energy from snacks but not meals (9). This implies that shortened sleep duration in modern societies may aggravate the problem of excessive energy consumption.

However, an observational cross-sectional study of Greek women ages 30-60 years using two 24-hour recalls, did not find that sleep duration was associated with energy intake or preference for fat and/or carbohydrate consumption (35). Yet, the same study suggests a direct association between shorter sleep duration and greater body fatness (35).

Another report on 12 healthy men looked at sleep duration influences on hormone levels. The daytime profiles of leptin and ghrelin were measured. Leptin levels were found to be stable across the daytime period which is consistent with the fact that calories were exclusively delivered in the form of constant glucose infusion. Sleep restriction relative to sleep extension was associated with a 24% increase in hunger ratings (19). Appetite increased by 23% as well as increases in consumed calorie dense foods with high carbohydrate content (p= 0.06) (19). This experimental study therefore suggest that
short sleep duration in young, healthy men is associated with decreased leptin levels, increased ghrelin levels, and increased hunger and appetite.

It is evident that lower leptin and higher ghrelin concentration increased hunger and appetite after short-term sleep restriction in healthy men (19). In the same study, increase in appetite was greatest for calorie dense food with high carbohydrate content and level of protein was not significantly affected by sleep duration. Likewise, another study to observe high glycemic index (GI) foods and Atkins diet in healthy men, linked sleep changes to the energy metabolism of fat (36). High GI foods delayed sleep onset which may be relevant to persons with sleep disturbance (36).

Weight Loss and OSA Improvement

A randomized clinical control trial to test whether successful weight reduction with lifestyle intervention would result in an improvement of mild OSA and its related morbidities concluded that lifestyle intervention with a very low calorie diet (VLCD) is a feasible low cost curative treatment for the vast majority of patients with mild OSA (13). In this study 72 consecutive overweight patients (18-65 years) with mild OSA were recruited. The intervention group received a year of lifestyle modification training with an initial weight reduction program where subjects were fed a VLCD (600-800 kcal/day) for 12 weeks, while the control group received routine lifestyle counseling. The intervention effectively reduced body weight and there was a significant difference in the mean change in AHI between the study groups. Changes in AHI were strongly associated with weight and waist circumference.
In a different study of 17 non-smoking, morbidly obese (body mass index, BMI 46-82 kg/m²) middle-aged men with documented OSA, there was a significant reduction of all anthropometric indexes including neck circumference and pharyngeal cross-sectional area after weight loss induced by an intragastric balloon for six months (15). This improvement was associated with a significant reduction of both the number of apnea episodes during sleep and daytime symptoms of OSA. The authors concluded that moderate weight loss was able to produce a short-term improvement in OSA in morbidly obese patients through modification of the upper airway size and patency (15).

Also, a prospective cohort study for twelve years that included 68,183 women aged 39-65 years and free of comorbid diseases reported a clear relationship between sleep duration and weight. Not only was a difference in baseline weight apparent but also weight increased more rapidly in those sleeping the least and this persisted over time. This finding suggests that short sleep duration is associated with a modest increase in future weight gain and incident obesity (14).

A longitudinal study using a community sample enrolled 2,968 middle-aged to older and moderately overweight men and women for three years. The Sleep Heart Health Study (SHHS) determined the average weight change was less during the five year follow up, but about five percent each of both men and women either gained or lost more than ten kilograms (37). The Respiratory Disturbance Index (RDI) is defined as the number of apnea plus hypoapnea events with at least a four percent oxyhemoglobin desaturation level divided by the total number of sleep also increased. By polysomnography the relationship between change in weight and progression or remission of sleep disordered breathing (SDB) was measured. Relative to the stable
weight individuals, weight gain in both men and women were more likely to result in an increase in their RDI. In adjusted models, weight gain in the same sex compared to stable weight individuals also had higher RDI (37). An important difference between men and women was noted in this study. Modest changes in weight were related to an increase or decrease in SDB, and this association was stronger in men than in women. Although women appear to have a different pattern and natural history of SDB than men, their conditions are still far more often under recognized and diagnosed relative to men and obesity remains a major risk factor for SDB (37).

Obstructive Sleep Apnea, Appetite and Macronutrient Intake

The direct relationship between Obstructive Sleep Apnea (OSA) and carbohydrate, protein and fat intake is complex and unknown to the researcher’s knowledge. Among the different studies reviewed, none has reported a relationship between dietary changes related to the macronutrients in subjects with OSA post CPAP treatment. Despite this, various researchers have suggested sleep restriction caused by OSA is significantly associated with hunger, increased BMI and increased cravings for carbohydrates, decreased leptin levels and increased ghrelin levels (19).

Also, preference for fatty foods has been documented. OSA is associated with fatigue and sleepiness which may curtail physical activity and result in a compensatory increase in caloric intake to boost energy level and therefore may promote weight gain. Based on this assumption, a randomized, double-blinded study of the relationship among dietary intake, physical activity and SDB was conducted. A study of 320 participants with severe SDB, half of whom were obese, showed a trend towards greater ingestion of
total calories, protein, fat, total saturated fatty acids, trans fatty acids and cholesterol but not carbohydrate, sucrose and dietary fiber (10).

Also, the researchers observed that individuals suffering from severe OSA were more likely to have unhealthy food habits (10). It is noteworthy that all the participants with extremely severe SDB consumed 88 milligrams more cholesterol per day as compared to those who had less severe OSA. The women with severe SDB, on average consumed 22, 28, and nine more grams of proteins, total fat and saturated fat, respectively.

This study provided new information on dietary habits in people with OSA indicating how SDB may lead to serious health conditions like CVD, hypertension and stroke (10).

Diet restriction alters sleep patterns. Despite the fact that low energy diets are an effective weight loss tool they are associated with physiological consequences that may not be beneficial. Weight loss in nine overweight premenopausal women between the ages of 20-36 years placed on a four week energy restricted diet (800Kcal/d,) resulted in delayed sleep onset and a decrease in slow wave sleep (38).

The Optimal Macronutrient Intake trial to Prevent Heart Disease (OMNI- heart) report stated appetite was lower on a protein-rich diet than on carbohydrate-rich or unsaturated fat-rich diets. This finding can be broadly applied and the appetite reducing effect of protein is lasting. This implies that diets having adequate protein content should be adopted as part of a healthy dietary regimen (39).

There was an experimental study conducted on subjects comparing weight loss with a high protein diet versus a moderate protein diet. The results showed that the
subjects in the high protein group achieved a greater weight loss within a 12 month timeframe. However, after 24 months both the high protein and moderate protein diet groups maintained their weight loss and reduced intra-abdominal fat stores (40).
CHAPTER III
RESEARCH DESIGN AND METHODS

Aim

To determine the relationship between Obstructive Sleep Apnea (OSA) improvement and changes in dietary intakes of total energy, fat, carbohydrate and protein..

Objectives

• To determine amount of macronutrient intake from existing dietary information collected with a food recall (24 hour recall). The dietary data were entered into Nutrition Data System for Research (NDSR) software, a standard contemporary nutrition program.

• To establish associations among existing data on demographic (age, sex), and sleep duration measurement and from the clinical trial study on ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome.’

• To find relationships and correlations between improvement in OSA and change in macronutrient intake at before and after treatment by data analysis in Microsoft excel 2007 version and JMP statistical tool.
Participants

This study used the availability of well-characterized secondary data from participants with sleep disordered breathing (SDB) recruited at the Dahms Clinical Research Unit (DCRU) in the clinical trial study on ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome’ by the Diabetes Association of Greater Cleveland (DAGC) and sponsored by Dietrich Diabetes Research Institute (DDRI). The subjects had untreated moderate to severe sleep apnea (AHI>15) and impaired glucose tolerance (IGT). They were chosen for this study because they fit into the criteria of individuals needed to test the hypothesis. This research project aimed at assessing the extent to which macronutrient intake changes with alterations in the severity of OSA after CPAP treatment.

The sleep apnea study was conducted from September 30, 2003 to September 29, 2007. Access to the data for the study were made available through collaboration with Dr. Susan Redline, principal investigator.

In order to protect these subjects’ privacy and confidentiality, the researcher signed a copy of the confidentiality certification and the Familial Aggregation and Natural History Study and Effects of Treatment of Sleep Apnea on Metabolic Syndrome data distribution policy. These agreements were endorsed by the principal investigator Dr. Susan Redline (Appendices A and B). Also, all questionnaires completed by subjects to be handled by the researcher had been previously coded. The researcher also completed an online course for Collaborative Institutional Training Initiative (CITI) and had a criminal background check.
Finally, to ensure compliance to research requirements the study had been previously approved by the Institutional Review Board (IRB) at the DCRU and The University of Akron (Appendix C).

Overview

This section briefly summarizes methodology of the research from which data was retrieved for this study. Moderate to severe OSA patients (AHI>15) were recruited at the DCRU in the clinical trial study on ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome’ by the DAGC. After two weeks of CPAP usage to test for compliance and to determine the inclusion criteria, all participants were discharged with no treatments for four weeks.

Baseline data (dietary, AHI and sleep duration) were collected during the fourth week of no treatment. The treatment groups were discharged with CPAP masks and controls with sham-CPAP. Eight weeks later CPAP treatment data were collected again and subjects were crossed over. Sleep duration measurement was taken during the seventh week of treatment (41). Sleep duration was assessed with a 7-day sleep diary and actigraphy. Actigraph was worn on the wrist for seven consecutive 24-hour periods. The polysomnography (PSG) was used to assess AHI.

Sample Size and Age

Data were available for a total of 53 subjects who were studied. The inclusion criteria for age was between 22-73 years who had moderate to severe SDB (AHI>15). It is important to note that dietary information analyzed were collected on two different visits hence a sum of 106 cases to be analyzed for the purpose of this study. This sample
size and age group were selected based on the fact that the sleep apnea and OSA is prevalent in the middle-aged population with a prevalence rate of about two to four percent (42).

Data Collection

Available demographic information was utilized by the researcher. The background information of the subjects on age and sex and medical information (sleep duration and AHI) were retrieved using established data existing from the Case Western Reserve University (CWRU) health and sleep questionnaire from the study “Effects of Sleep Apnea Treatment on Metabolic Syndrome”.

Likewise, dietary information on study subjects were assessed from 24 hour food recalls responded to by the subjects on multiple visits. A copy of the food recall form that was used is attached in Appendix D.

The body mass index (BMI) was calculated from weight (kilograms) divided by height in meters squared and was determined from the existing anthropometric data (height and weight) available in the data set.

Data Analysis

Using descriptive statistics (frequencies, percentages, means, and standard deviations), all information were summarized and displayed in tables and graphs for each variable and key bivariate relationship. This provides simple summaries about the sample and presents quantitative descriptions in manageable form for demographics, anthropometric, medical and nutrition data (carbohydrates, fats and protein consumed as percentage kilocalories and grams per day).
Initial models described associations of dietary parameters with indices of SDB, using data from each time-point (baseline and Post-CPAP) in separate analyses. Correlations found the degree of relation between any two variables.

In order to determine significant relationships among the different variables paired t-test were used. Each macronutrient relationship was determined by paired t-test analysis at baseline and Post CPAP. In addition, data were subdivided into different groups such as males versus females, Caucasian versus African American, and before and after CPAP treatment.

Diet

Dietary recall data were entered by the researcher at University Hospitals in Cleveland, Ohio and nutrients calculated by Nutrition Data System for Research (NDSR). The NDSR is a windows-based dietary analysis program designed for the collection and analyses of 24-hour dietary recalls. With the NDSR software, calculation of nutrients occur immediately providing data per ingredient, food, meal, and day, in report and analysis file formats (43). It also possesses high quality, comprehensive and complete nutrient data, extensive specificity for food variables and preparation methods, timely addition of nutrients and food components of scientific importance (43).

Hypothesis 1: Improvement in OSA is correlated with a change in total energy intake.

Various clinical observations throughout the United States, Europe, Asia and Australia conducted in the 20th century, have established excess weight as a predictor of SDB. A study that compared moderate OSA (AHI≥5) and severe OSA (AHI≥15) patients
found a greater proportion of the later is attributable to weight (44). Since there was no statistically significant difference in BMI at baseline and post-CPAP it was not necessary to adjust the data for weight.

Paired t-test analyses and linear correlations were used to determine baseline to post-CPAP differences and relationships in total energy intakes, OSA levels, percentages of specific macronutrient intakes and other variables. Paired t-test is a standard method used to compare means on the same or related subject over time (45). The method produces precise results and reduces bias since the variables to be compared are balanced, therefore cannot distort the comparison.

In this study, the change in total energy intake was found using the JMP statistical tool that determined the change in total energy intake (kcal) at baseline minus post-CPAP treatment for all participants. Correlation graphs and paired t-test were outcomes that helped the researcher to draw conclusions.

Hypothesis 2: Improvement in OSA is correlated with a change in the proportion of total energy consumed as fat, protein and carbohydrate.

The statistical data were treated the same as described in hypothesis I. The difference between total energy consumed as percentage calories of fat, carbohydrate and proteins at baseline and after eight weeks of CPAP treatment is the focus. This was to enable the researcher to know if there was a change in the proportion of total energy consumed as fat, protein and carbohydrate in relation to post CPAP and baseline treatment.
Limitations

A 24 hour recall was used to collect dietary information which does not provide accurate and unbiased estimates of an individual’s energy intake. The percentage of people who underestimate or overestimate their food intake range from 10 to 45 depending on age, sex and body composition (46). Women and obese tend to underestimate their intakes (46). The subjects may have over- or under-reported their dietary intake because of previous nutrition knowledge, and may not have reported accurate portion sizes of foods eaten. Again, it is difficult to determine whether the day being recalled represents an individual’s typical intake.

It is possible that the length of CPAP treatment was not long enough for this study, taking into consideration it requires time to change dietary habits and intake and also for the body to adjust to new habits. The sample was small whereas a larger sample size will increase precision.

The secondary data used had some missing information which needed to be accounted for. For instance baseline data for three subjects were missing and sham-CPAP measurements were used as baseline data. Also, the NDSR 2007 software actually records the dietary information while the subject is been interviewed. In this study, the researcher did not have this privilege, and the data were collected prior to 2007. Moreover, not all foods are represented in the NDSR software and the closest food needed to be chosen if the specific food item was not found. Some dietary data entered was based on memory recall from the nutrition assistants who recorded the 24-hour recall.
CHAPTER IV
RESULTS AND DISCUSSION

Introduction

This research focused on individuals with moderate to severe obstructive sleep apnea (OSA) enrolled in an existing study from the clinical trial study on ‘Effect of Sleep Apnea Treatment on Metabolic Syndrome’. The main objective was to determine if an improvement in OSA is associated with a change in total energy intake. A second objective was to determine if an improvement in OSA is related to an alteration in the proportion of dietary carbohydrate, protein and fat consumed. According to various studies, individuals with OSA tend to consume higher energy intakes and have less healthy eating habits (37). Therefore, it was expected that after eight weeks of CPAP treatment for OSA, that total energy intake would decrease.

Data Analysis

Fifty-three subjects with moderate to severe (OSA) participated in this study. Dietary information was recorded with a 24-hour recall on two different visits, at baseline and after CPAP treatment. The dietary information was input into NDSR which determined the quantity of each nutrient in standard units of measurement. Focusing on the purpose of this study, only total energy and macronutrients consumed in grams and
as percentage kilocalories per day were used. Other parameters of interest included sleep duration, age and apnea-hypopnea index (AHI).

Population

The racial make-up of this study consisted of 33 whites (62.0%) and 20 black (38%). The majority were white females. There were 31 females (58.5%) and 22 males (42.0%) participating in the study. Sub-categories include 19 white females (35.8%) and the eight black males (15.0%), Figure 4.1. The number of white males and black females were approximately a quarter of the population, 26.4% and 22.6%, respectively.

![Figure 4.1](image)

**Figure 4.1.** A representation of participants by gender and race.

Demographics and Medical Information

The mean sleep duration was $6.23 \pm 0.99$ hours at baseline and after eight weeks of CPAP treatment, $6.09 \pm 0.91$ (p=0.471). The mean BMI was $38.87 \pm 8.97$ at baseline
and 38.74 ± 8.81 post CPAP. Mean AHI was 37.75 ± 23.60 at baseline and 3.31 ± 7.28 post CPAP. The mean age (years) of participants (n=53) was 53.87 ± 9.70 at baseline.

The correlations and p-values for BMI and AHI are (r=0.061; p=0.946) and (r=0.027; p<0.0001) respectively. The researcher realized that BMI (and/or weight) should be considered when assessing dietary intake. However, since no statistically significant differences in BMI (weight) were found, it was not necessary to do a statistical adjustment of the data.

Table 4.1. Baseline and Post-CPAP Treatment for Participants with Moderate to Severe OSA

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean ± S</th>
<th>Post-CPAP Mean ± SD</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep time (hours)</td>
<td>6.23 ± 0.99</td>
<td>6.09 ± 0.91</td>
<td>-0.1156</td>
<td>0.4710</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>38.87 ± 8.97</td>
<td>38.74 ± 8.81</td>
<td>-0.0614</td>
<td>0.9462</td>
</tr>
<tr>
<td>AHI</td>
<td>37.75 ± 23.60</td>
<td>3.31 ± 7.28</td>
<td>0.0271</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.87 ± 9.70</td>
<td>54.13 ± 9.70</td>
<td>0.0892</td>
<td>0.8840</td>
</tr>
</tbody>
</table>

Note. SD-standard deviation
r-pearson correlation of the relationship of baseline to post-CPAP for each category
p-value are for t-test of comparisons between groups.

Dietary Information

The average total energy intake and macronutrient intakes summarized in the Table 4.2 below show that men had slightly higher energy post-CPAP treatment, although not significant. There were no significant differences observed for energy in kcal (r=-0.105; p=0.359), in grams fat/day (r=-0.478; p=0.529), grams carbohydrate/day (r=0.176; p=0.312) and grams proteins/day (r=-0.268; p=0.545). In women, there were no significant changes in total energy intakes or macronutrient intakes (in grams) when
comparing baseline to post-CPAP treatment. Energy in kcal \((r= -0.193; p=0.729)\), in grams fat/day \((r=0.000; p=0.778)\), grams carbohydrate/day \((r=-0.374; p=0.390)\) and grams proteins/day \((r=0.022; p=0.660)\). Although not significant men tended to consume higher amounts of nutrients than women, as would be expected due to their greater energy needs.

Table 4.2. Macronutrient Intake (Kcal/day) by Gender at Baseline and After CPAP Treatment

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Mean ± SD Baseline</th>
<th>Mean ± SD CPAP</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal/day)</td>
<td>1966.38 ±664.44</td>
<td>2180.59 ±773.61</td>
<td>-0.105</td>
<td>0.359</td>
</tr>
<tr>
<td>Fat (g/day)</td>
<td>84.17 ± 26.67</td>
<td>91.36 ± 34.35</td>
<td>-0.478</td>
<td>0.529</td>
</tr>
<tr>
<td>Fat (% kcal/day)</td>
<td>39.06 ± 7.44</td>
<td>38.18 ± 9.48</td>
<td>-0.015</td>
<td>0.738</td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>226.61 ±119.31</td>
<td>261.84 ±129.15</td>
<td>0.176</td>
<td>0.312</td>
</tr>
<tr>
<td>Carbohydrate, % kcal</td>
<td>44.83 ± 11.26</td>
<td>47.04 ± 9.95</td>
<td>0.096</td>
<td>0.476</td>
</tr>
<tr>
<td>Proteins (g/day)</td>
<td>79.79 ± 27.43</td>
<td>86.08 ± 32.64</td>
<td>-0.268</td>
<td>0.545</td>
</tr>
<tr>
<td>Protein, % (kcal/day)</td>
<td>16.79 ± 5.49</td>
<td>16.14 ± 3.80</td>
<td>0.025</td>
<td>0.608</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy (kcal/day)</td>
<td>1755.98 ±506.76</td>
<td>1807.66 ±559.03</td>
<td>-0.193</td>
<td>0.729</td>
</tr>
<tr>
<td>Fat (g/day)</td>
<td>79.04 ± 30.31</td>
<td>76.94 ± 27.49</td>
<td>0.000</td>
<td>0.778</td>
</tr>
<tr>
<td>Fat (% kcal/day)</td>
<td>39.89 ± 8.65</td>
<td>38.67 ± 7.98</td>
<td>-0.034</td>
<td>0.575</td>
</tr>
<tr>
<td>Carbohydrate (g/day)</td>
<td>185.51 ± 62.41</td>
<td>205.08 ± 87.47</td>
<td>-0.374</td>
<td>0.390</td>
</tr>
<tr>
<td>Carbohydrate, % kcal</td>
<td>42.54 ± 10.88</td>
<td>44.76 ± 10.33</td>
<td>-0.060</td>
<td>0.429</td>
</tr>
<tr>
<td>Proteins (g/day)</td>
<td>80.61 ± 25.49</td>
<td>77.58 ± 28.89</td>
<td>0.022</td>
<td>0.660</td>
</tr>
<tr>
<td>Protein, % (kcal/day)</td>
<td>18.81 ± 5.49</td>
<td>17.74 ± 5.13</td>
<td>-0.112</td>
<td>0.458</td>
</tr>
</tbody>
</table>

Note. SD-standard deviation

\(r\)-pearson correlation of the relationship of baseline to post-CPAP for each category

\(p\)-value are for t-test of comparisons between groups.

Improvement OSA and Dietary Intake Changes

The measure of strength and direction of the relationship between OSA change and change in energy (kcal) (Figure 4.2), change in percentage kcal as fat (Figure 4.3), carbohydrate (Figure 4.4) and protein (Figure 4.5) is shown in the following figures. The
changes in the nutrients (total energy, fat, carbohydrate and protein) and OSA were calculated as values obtained at baseline minus the values obtained after eight weeks treatment with CPAP (Post-CPAP). All values below the blue line represent a higher intake after CPAP treatment and vice versa.

The mean change with improvement in OSA for total energy (kcal) is -68.57, fat (%kcal/day) is 1.07, carbohydrate (%kcal/day) is -2.19 and protein (%kcal/day) is 0.84. As OSA improved there was a slight but non-significant increase in the total energy (kcal) consumed as shown in Figure 4.2. As OSA improved there was a statistically significant increase in the percentage of kcal consumed as fat (p=0.04) (Figure 4.3). Although not statistically significant, as OSA improved the percentage of kcal consumed as carbohydrate and protein (%kcal/day) decreased as shown in Figures 4.4 and 4.5 respectively.

Figure 4.2. The relationship between change in energy intake (kcal/day) and the change in OSA.
Figure 4.3. The relationship between change in percent fat intake (kcal/day) and the change in OSA.

Figure 4.4. The relationship between change in percent carbohydrate intake (kcal/day) and the change in OSA.
Figure 4.5. The relationship between change in percent protein intake (kcal/day) and the change in OSA.

Although the relationship is weak, there was a significant increase in the percent of kcal consumed as fat \( (r = -0.276; p=0.046) \) with improvement in OSA. In Table 4.3 it is observed that there is a strong negative relationship between change in fat and carbohydrate \( (r = -0.800; p<0.0001) \). Likewise, there is a significant negative relationship between change in total energy intake (kcal/day) and change in percent of kcal consumed as protein \( (% \text{ kcal/day}) \) \( (r=0.362, p=0.008) \).
Table 4.3. Improvement in OSA and Its Association with Change in Percentage Fat, Carbohydrate and Protein (kcal/day)

<table>
<thead>
<tr>
<th>Parameters</th>
<th>BMI (Kg/m²) baseline</th>
<th>OSA change</th>
<th>Energy (kcal) change</th>
<th>Percentage Kcal/day change</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>r=0.111</td>
<td>r=-0.031</td>
<td>r=-0.110</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.430</td>
<td>p=0.826</td>
<td>p=0.432</td>
</tr>
<tr>
<td></td>
<td></td>
<td>r=0.102</td>
<td>r=-0.036</td>
<td>r=-0.276</td>
</tr>
<tr>
<td></td>
<td></td>
<td>p=0.466</td>
<td>p=0.466</td>
<td>p=0.762</td>
</tr>
<tr>
<td>OSA change</td>
<td>r=0.111</td>
<td>p=0.430</td>
<td>r=-0.036</td>
<td>r=-0.276</td>
</tr>
<tr>
<td></td>
<td>p=0.430</td>
<td>r=0.197</td>
<td>r=0.181</td>
<td>r=-0.037</td>
</tr>
<tr>
<td></td>
<td>p=0.762</td>
<td>p=0.008</td>
<td>p=0.008</td>
<td>p=0.047</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>r=0.031</td>
<td>p=0.826</td>
<td>p=0.798</td>
<td>p=0.008</td>
</tr>
<tr>
<td></td>
<td>p=0.798</td>
<td>r=0.181</td>
<td>r=0.196</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>% Cal Fat change</td>
<td>r=-0.110</td>
<td>p=0.432</td>
<td>p&lt;0.0001</td>
<td>p=0.047</td>
</tr>
<tr>
<td>% Cal CHO change</td>
<td>r=0.102</td>
<td>p=0.466</td>
<td>p&lt;0.0001</td>
<td>p=0.032</td>
</tr>
<tr>
<td>% Cal Protein change</td>
<td>r=0.043</td>
<td>p=0.762</td>
<td>p=0.008</td>
<td>p=0.047</td>
</tr>
</tbody>
</table>

Note. r-pearson correlation coefficient

Discussion

The present study examined the relationship between OSA improvement and change in total energy intake (kcal). In addition, change in OSA was correlated with changes in the proportion of total energy consumed as fat, carbohydrate and protein.

Previous studies have concluded that there is a significant association between elevated weight, BMI and OSA (15, 21, 22, 37). Although weight (BMI) is associated with OSA, the current study found no change in weight after AHI improved. Because of this finding no statistical adjustment for weight was made.

OSA Improvement and Change in Total Energy Intake (kcal)

The results from Figure 4.2 show that improvement in OSA was not associated with a change in total energy intake. As represented in Table 4.3, an improvement in
OSA and its association with energy intake (kcal) was not significant ($r = -0.036; p = 0.798$) and the mean change in total energy intake was -68.57 (kcal/day). On average, all participants consumed less than the estimated energy requirement (EER) of 3067 and 2403 kcal/day for an active adult male and female, respectively (46). However, the EER may not be representative for this group of participants. The activity level and other factors responsible for variation in energy needs were not measured in the current study.

Data from a previous study of people with moderate to severe OSA showed a 67% decrease in AHI as compared with controls after seven weeks of treatment with a very low calorie diet (VLCD) (47). The subjects with severe OSA at baseline had a more significant reduction in AHI than those with moderate sleep apnea (47). Furthermore, there was a significant change in AHI when subjects were fed 600 to 800 kcal/day of a VLCD for 12 weeks (13). The researcher of the current study expected that perhaps the converse is true, that a decrease in AHI after eight weeks of CPAP treatment could be associated with a decrease in the total energy intake (kcal/day). However no significant change in energy intake was observed.

Also, it was thought by the researcher that with successful OSA treatment caloric intake would adjust downward to promote appropriate weight. While it has been shown that AHI may be reduced with reduced energy intake, the converse (lowered caloric intake with reduced AHI) was not found in the current study.

The high fat intake in the current study could be a factor for maintaining energy intakes after CPAP treatment. Research has shown that fat intake that exceeds 35% of total calories is associated with higher caloric intake (48). In the current study, all
subjects chose a diet high in fat exceeding 35% of total calories, during baseline and post-CPAP (Table 4.2).

The lack of a change in energy intake after eight weeks of CPAP treatment may be due to many factors influencing food choices. A positive dietary habit requires time to develop and may not be seen immediately following reduction in AHI and after only eight weeks of treatment. The duration of the current study may have not been sufficiently long enough to observe a significant dietary change. Perhaps with a longer study duration a significant change might be observed.

Also, the method of dietary data collection is not the actual representation of the participant’s diet since food intake varies from day to day, and only two 24-hour recalls were collected. It is worth mentioning that the 24-hour recall is a quick and simple method to collect dietary intake but its documented limitations may have had an adverse effect on this study. This method of dietary collection relies on patient memory to accurately recall foods eaten and portion sizes. Also, the information provided may not be a true account of the usual dietary intake of the participant. The individual’s usual food habits, eating patterns and identification of other factors that influence nutrient intake may not be captured by a 24-hour recall (46).

To increase the accuracy of dietary intake assessment, multiple methods may be used to collect dietary data. The 24-hour recall could be used together with a food frequency questionnaire which provides more precise estimation of intake (46). This is because the food frequency questionnaire documents the frequency of usage of food groups while the 24-hour recall allows the analysis of specific nutrients (46).
Alternatively, a 7-day food record may also be used as it provides nutrient information averaged at the end of a seven-day period (46).

**Sleep Duration and Its Relationship to Energy Balance**

Considering sleep duration, it is important to note that in Table 4.1 there was no improvement at post-CPCP compared to baseline, although AHI decreased with treatment. The average sleep time was approximately six hours in the current study. The sleep duration was expected to be longer than six hours after AHI significantly improved since other research findings in the United States, Europe and Asia have reported short sleep duration is a consequence of OSA (4, 7, 49).

Sleep duration could have an influence on energy intake. Previous research showed that shortened sleep duration increased hunger by 24% and appetite by 23% promoting ingestion of calorie dense foods in healthy men (19). On the contrary, another study in middle-aged Greek women did not find a relationship between sleep duration and energy intake (35). Based on these reports it is not surprising that energy intake was not altered after treatment in the current study, since no change in sleep duration was found.

Shortened sleep duration could affect the appetite controlling hormones, leptin and ghrelin. To confirm this, a study that intentionally reduced sleep to four hours for six consecutive nights and then extended to 12 hours for six consecutive nights, found a decrease in leptin levels and increased hunger and appetite with restricted sleep (19). Leptin and ghrelin levels were not available in the current study but would have been helpful for interpreting the study results.
Ghrelin and leptin levels have been studied in people with OSA (50). Thirty obese men 35 years and older with severe OSA (AHI>30) and their matched control group whose ghrelin and leptin levels were recorded eight weeks after onset of CPAP showed a marked decrease in plasma leptin levels (50). The results were more pronounced in those with BMI < 30 than in those with BMI >30. This is consistent with another research study on people with OSA that concluded that leptin levels decreased only in non-obese participants with CPAP treatment (32). Again, another study revealed that after a year of CPAP treatment in OSA participants (mean age 55.4 + 12 years), there was no significant change in BMI in the obese subjects, but BMI significantly increased in non-obese subjects p=0.044 (51). From the above findings it is not surprising to observe that CPAP treatment did not have an impact on BMI in the current study, since all participants were obese.

OSA Improvement and Change in Proportion of Total Energy Consumed as Fat, Protein and Carbohydrate

In Table 4.3, a direct association between OSA change and change in calories as percent fat was observed. As improvement in OSA increased, the change in total energy consumed as fat as percent of kcal per day increased significantly (r= -0.276; p =0.046). Also, the average percent fat intake (close to 40% of kcal) was above typically recommended consumption (Table 4.2). The Acceptable Macronutrient Distribution Range (AMDR) is 20-35% (48).

However, carbohydrate and protein intake (percent kcal/day) did not change with improvement in OSA as shown in Figures 4.4 (r=0.197; p=0.157) and 4.5 (r=0.147; p=0.294), respectively. All the subjects consumed more than the Recommended Dietary
Allowance (RDA) set for both macronutrients but were within the AMDR range (Appendix E, 48).

A study that derived data from the “Apnea Positive Pressure Long-term Efficacy Study” (APPLES) found that an increased severity of OSA was associated with greater ingestion of total calories, fat and protein but not carbohydrates (10). The same study also found that women who had severe OSA consumed 27.75 and 21.96 more grams of fat and proteins, respectively (10). Conversely, another study reported sleep restriction caused by OSA to be associated with cravings for carbohydrates (19).

The increase in percentage fat consumed with OSA improvement is more difficult to explain. The relationship between fat intake and improved OSA has not been reported in the literature, to the knowledge of the researcher. However, an increase in percent fat intake must be associated with a decrease in either percent protein or percent carbohydrate consumed, or both. According to the results in Table 4.3, change in kcal as fat was significantly negatively correlated with percentage kcal change as carbohydrates ($r= -0.800, p<0.0001$) and percentage kcal change as protein ($r= -0.272, p= 0.047$). However, change in percent kcal as carbohydrate was not found to be significantly directly associated with OSA improvement in the current study. More research is needed to better understand the relationships between the macronutrients and improved OSA.

A decrease in percentage of carbohydrate consumed with improvement in OSA was anticipated by the researcher, since OSA is associated with carbohydrate craving (19). Based on this finding it could be hypothesized that when OSA improves carbohydrate intake could decrease. However, a non-significant association in percent kcal as carbohydrate with OSA improvement was the outcome of the current study.
High fat diets may be credited to palatability which is induced by innate responses and learning. The content of the subjects’ diets may be an important factor in this research rather than the amount of food consumed because food intake is usually driven by hunger and external stimuli. This study was influenced by many factors including sleep duration, OSA, OSA improvement, AHI, study duration, number of participants and likely hormonal influences.

Limitations of the Study

The limitations associated with a 24-hour recall cannot be underestimated in the current study. The inaccuracies associated with it include over-reporting low intakes or under-reporting high intakes (46). For instance, it is reported that women and obese individuals tend to underestimate their food intake (46). In addition, the portion sizes and foods eaten are often not interpreted correctly by the participant or interviewer.

The Nutrition Data System for Research (NDSR) is a valuable tool, however not all foods are represented in this system. During data entry, the researcher chose foods closest to what was reported on the 24-hour recall. Food content varies no matter how closely related they may be, hence some variation in the true representation of the actual dietary content consumed may be observed.

Another limitation of this study is the lack of additional measures related to energy intake. For instance, data on the activity level and appetite controlling hormones leptin and ghrelin were not available. Also three baseline data were missing; therefore sham-CPAP data was used as baseline information. These participants were not
eliminated from the analysis because it was assumed that the sham-CPAP was similar to baseline data.

Considering that change in food habits occurs over time, a rapid change in total energy and macronutrient intake may not be associated with an immediate improvement in OSA. Practiced habits require cognitive restructuring, life style modification and self-monitoring to avoid unhealthy dietary choices and food consumption. Hence, the length of the study may not have been long enough to evaluate the possibility of significant change in dietary macronutrient intake with OSA improvement.

Summary

Overall, this study found that improvement in OSA (reduced AHI) was associated with a significant increase in the percentage of fat intake. However, there was no change in total energy or in percent kcal/day of carbohydrate and protein intakes with OSA improvement. Other studies found that VLCD is associated with decreased OSA severity (13, 47). Also, another study reported an association between OSA severity and higher total caloric intake, fat, protein but not carbohydrate (10). To the knowledge of the researcher the association between improvement of OSA and changes in macronutrient intake has not been studied previously.

Additionally, other studies showed that reduced sleep duration is related to increased hunger and appetite, increased total caloric, carbohydrate, fat intakes and decreased leptin levels, which promote obesity over time (19, 31, 33). Although the researcher predicted an alteration in sleep duration after OSA improvement, no significant association was found in the current study. The importance of sleep cannot be
underestimated in nutrition research, though, due to the association of short sleep
duration and obesity (14).

Food intake and choices are shaped by many factors including socio-cultural,
physiological and cognitive influences. An immediate change in dietary intake was not
likely to occur in the short period of the current study because food habits and choices are
adaptive traits over time. The duration of this study may have not been sufficient to
observe significant change in many of the variables studied. Another limitation is the use
of the 24-hour recall that reflected intake for only one day at baseline and one day post-
treatment, which may not be a true representation of an individual’s usual intake.
CHAPTER V

SUMMARY

Statement of Problem

The purpose of the current study was to investigate relationships between macronutrient intake and improvement in OSA as evidenced by a reduction in AHI. In addition, macronutrient intake, sleep duration and AHI at baseline and post-CPAP treatment were measured and compared.

OSA may cause sleep duration to be shortened due to arousals in sleep that occurs with the condition. Reduced sleep can affect the appetite regulating hormones leptin and ghrelin which help to moderate food intake. These alterations in sleep can lead to appetite regulating hormone disruption and obesity (14, 19). Obesity is a risk factor for OSA. However, OSA and obesity are both independently linked to cardiovascular disease morbidity and mortality in the United States (27).

Since individuals with OSA tend to be obese, dietary factors such as overconsumption of total calories or changes in relevant macronutrient proportions are likely to contribute to these conditions. Similarly, dietary factors may be important components in the treatment of OSA. Therefore improved understanding of these relationships is essential.
Summary of Hypotheses

The current study hypothesized that an improvement in OSA (decreased AHI) could have a positive influence on the amount of nutrients consumed as fat, carbohydrate and protein. However, the statistical analysis showed that OSA improvement did not have an alteration in energy intake (kcal/day). However, there was an increase in the proportion of total calories consumed as fat as OSA improved, but the percentage of calories as carbohydrate and protein was not altered. The relationships between dietary intake and OSA improvement are not well understood. Further studies should be done to investigate more clearly the specific relationships between diet components and OSA amelioration, and the potential of incorporating medical nutrition therapy into the treatment of OSA.

Implications

This study has demonstrated that dietary intake does not change significantly with improvement in OSA after CPAP treatment. However, it has been revealed that an increase in percent fat intake occurred with improved OSA. It may be of interest to nutrition researchers to find out why the percent of dietary fat intake increased with OSA improvement. Nutrition professionals may consider placing an emphasis on adequate sleep in addition to other weight loss recommendations.

This research has added to the nutrition knowledge and its potential impact on OSA improvement. Although, nutrition is directly related to obesity and likewise obesity to OSA, OSA improvement is indirectly related to both. The current findings may assist
future researchers in focusing studies on the direct relationships between macronutrient intake and OSA improvement.

Possibilities for Future Research

Future studies may use multiple dietary collection methods (food frequency questionnaire, food diary and nutrient intake record) for a better representation of the participant’s usual dietary intake. Also, data on activity level and appetite controlling hormones would enhance future studies. In addition, analysis on the specific source of fat from the diet would be valuable. This is because total fat is comprised of essential and non-essential fatty acids, saturated and unsaturated fatty acids. Analysis of the sources of carbohydrate and protein could be useful as well.

Since dietary change occurs over time, the study duration could be extended and the sample size increased. The increased percent fat intake with OSA improvement is not well understood. It is worth investigating this observation further. This is important because high fat diets are associated with obesity and obesity is associated with OSA.
REFERENCES


APPENDIX A

NOTICE TO KEEP RESEARCH DATA CONFIDENTIAL

Effects of Treatment of Sleep Apnea on Metabolic Syndrome

CONFIDENTIALITY CERTIFICATION

As an employee of, consultant to, or fellow/student involved with the Effects of Treatment of Sleep Apnea on Metabolic Syndrome (CPAP Metabolic Study) funded by the National Heart, Lung, and Blood Institute (NHLBI), I am aware of the confidential nature of data on research participants maintained by the Study, and of the necessity for maintaining that confidentiality.

I agree not to transfer or disclose any confidential data, nor any information about individuals CPAP Metabolic Study participants, except as necessary for data/safety monitoring or programmatic management, in the course of my responsibilities at work or in private, either during or after any affiliation with the CPAP Metabolic Study. I agree not to transfer any CPAP Metabolic Study data to individuals outside the CPAP Metabolic Study Group without the written permission of the Principal Investigator, Susan Redline. Further, I agree to return all CPAP Metabolic Study data to the Principal Investigator (SI) or delete/destroy all CPAP Metabolic Study data upon termination of my affiliation with the Study.

I understand that as an employee of, consultant to, or fellow/student involved with a study funded by the United States Government, I am subject to the provisions of 5 U.S.C. 552a governing federally maintained records on individuals. 5 U.S.C. 552a(1)(A) imposes criminal penalties on any federal officer or employee “who by virtue of his employment or official position, has possession of or access to, agency records which contain individually identifiable information the disclosure of which is prohibited by this section or by rules or regulations established thereunder, and who knowingly discloses the material in any manner to any person or agency not entitled to receive it. Recipient may be fined up to $10,000, imprisoned up to one year, or both. Reckless disclosure of personal information contained in Study records.

Name (print): Nao Kraduch Anreah

Signature: [Signature]

Date: 02/10/09

Principal Investigator’s Signature: [Signature]

Date: 03/19/9
APPENDIX B

AGREEMENT AND APPROVAL TO USE RESEARCH DATA FROM THE EFFECT OF TREATMENT OF SLEEP APNEA ON METABOLIC SYNDROME STUDY

AGREED TERMS AND CONDITIONS

It is mutually agreed as follows:

1. **Research Project**

   1.1. The data will be used by Recipient's Principal Investigator solely in connection with the following research project ("Research Project"), specifically described below or in an attached Exhibit A:

   1.2. The Research Project involves the following Family Sleep Study Investigators (co-investigators): The work they will perform is described below or in an attached Exhibit B:

   1.3. The Distribution Agreement covers only the above-described Research Project. Recipient will submit a completed Distribution Agreement (this document) for each research project for which the data are requested.

2. **Non-transferability**. This Distribution Agreement is not transferable. Recipient agrees that substantive changes made to the Research Project described above, and/or appointment of another Principal Investigator to complete the Research Project, require execution of a new Distribution Agreement which the new Principal Investigator and/or new Research Project are designated.

3. **Publication**. Prompt publication or any public disclosure of the results of the Research Project is encouraged. Recipient agrees to provide to the Principal Investigator a copy of any manuscript or other disclosure document within thirty (30) days of submission for publication, in order to ensure compliance with the confidentiality requirements set forth in paragraphs 4, 5, 6, 7, and 8 of this Agreement.

4. **Acknowledgments**. Recipient agrees to acknowledge the contribution of the Family Sleep Study investigators in any and all oral and written presentations, discussions, and publications resulting from any and all analyses of Data.

   4.1. **Collaborators**. Recipient will acknowledge the Family Sleep Study Investigators in any public presentation, discussion, and publication resulting from any and all analyses of Data.

5. **Non-use**. Recipient agrees that Data will not be used in any research field not used described and approved as part of the Research Project.
6. Use Limited to Research Project. Recipient agrees that Data will not be used in any research that is not disclosed and approved as part of the Research Project.

7. No Distribution. Recipient agrees to retain control over Data, and further agrees not to transfer Data, with or without charge, to any other entity or any individual. Recipient agrees that when the Research Project is completed, or three (3) years have elapsed from the effective date of this Distribution Agreement, whichever occurs first, the data will be either returned to the Family Sleep Study/Metabolic Study Investigator or deleted/destroyed as mutually agreed upon, unless an extension of this agreement is obtained.

8. Termination. Family Sleep Study may terminate this Distribution Agreement if Recipient is in default of any condition of this Distribution Agreement and such default has not been remedied within 30 days after the date of written notice by Family Sleep Study Principal Investigator of such default. Upon termination of their Distribution Agreement, Recipient agrees to either return all the Data to the Study Investigator or delete/destroy all Data as mutually agreed upon.

9. Accuracy Representation. Recipient expressly certifies that the contents of any statements made or reflected in this document are truthful and accurate.

This Distribution Agreement is entered into as of: 03/09/09 (effective date)

RECIPIENT ORGANIZATION

Name of Recipient Organization: University of Akron

Name and Title of Recipient's Authorized Representative: Dr. Hinda Khana (Co-Principal Investigator)

Signature and Date of Recipient's Authorized Representative: 

Recipient E-Mail Address: 

Recipient Telephone Number: 230-183-4425

Recipient Fax Number: 230-183-4425

Family Sleep Study/Metabolic Sleep Study Authorized Investigator:

Name and Title of Family Sleep Study/Metabolic Sleep Study Authorized Investigator: 

Signature and Date of Family Sleep Study/Metabolic Sleep Study Authorized Investigator: 

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APPENDIX C

THE UNIVERSITY OF AKRON INSTITUTIONAL REVIEW BOARD APPROVAL LETTER

NOTICE OF APPROVAL

Date: September 3, 2009

To: Naokazu Kabashima

1935 Erie Place

Akron, OH 44366

From: Sharon Huhtala, IRB Administrator

Re: IRB Number 2079007 “The Association between Sleep Duration and Micronutrient Intake in Adults with Obstructive Sleep Apnea”

Thank you for submitting your Exemption Request for the referenced study. Your request was approved on September 3, 2009. The protocol represents minimal risk to subjects and matches the following federal category for exemptions:

☐ Exemption 1 - Research conducted in established or commonly accepted educational settings, involving normal educational practices.

☐ Exemption 2 - Research involving the use of educational tests, survey procedures, or observations of public behavior.

☐ Exemption 3 - Research involving the use of educational tests, survey procedures, or observations of public behavior not exempt under category 2, but subjects are selected or assigned to the research by their parents or legal guardian.

☐ Exemption 4 - Research involving the collection of existing data, documents, records, psychological specimens, or diagnostic specimens.

☐ Exemption 5 - Research and demonstration projects conducted by or subject to the approval of department of agency head, and which are designed to study, evaluate, or otherwise examine public programs or benefits.

☐ Exemption 6 - Taste and food quality evaluation and consumer acceptance studies.

Annual continuation applications are not required for exempt projects. If you make changes to the study's design or procedures that increase the risk to subjects or involve activities that do not fit within the approved exemption category, please contact the IRB staff whether or not a new application must be submitted. Any such changes or modifications must be reviewed and approved by the IRB prior to implementation.

Please retain this letter for your files. If the research is being conducted for a master's thesis or doctoral dissertation, the student must file a copy of this letter with the thesis or dissertation.

CC: Deborah Martin - Advisor

CC: Stephanie Woods - IRB Chair

Office of Research Services and Sponsored Programs

Phone: 330-972-5880 • Fax: 330-972-5881

The University of Akron - Board of Trustees and Institutional Review Board
### APPENDIX D

**DIETARY INTAKE ASSESSMENT WITH 24-HOUR RECALL**

#### 24-Hour Food Recall

Personid: ___________  NameCode: ___________  Date of Birth: ___________  Tech id: ___________

Today’s Date: __/__/____  Day of the Week: ___________  Recall Date: __/__/____  Recall Day of the Week: ___________

Was the recall day a typical day? ___________

Day of recall, child at school or work? No or Yes (circle)

Day of recall, parents/guardians at work? One, Both, or Neither (circle)

<table>
<thead>
<tr>
<th>Time</th>
<th>Meal Type</th>
<th>Food, Beverage, and Supplements</th>
<th>Brand Name</th>
<th>Amount Eaten (please specify units: cups, tbsp, or...)</th>
<th>Toppings, Condiments, and Add Ins</th>
<th>How was item prepared?</th>
<th>Prepared By</th>
<th>Eaten Where</th>
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<td>Food, Beverage, and Supplements</td>
<td>Brand Name</td>
<td>Amount Eaten (please specify units- cups, tbsp, oz...)</td>
<td>Toppings, Condiments, and Add Ins</td>
<td>How was item prepared?</td>
<td>Prepared By</td>
<td>Eaten Where</td>
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### APPENDIX E

THE DIETARY REFERENCE INTAKE FOR AMERICANS

#### Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals, Macronutrients

<table>
<thead>
<tr>
<th>Life Stage Group</th>
<th>Total Carbohydrate (g/d)</th>
<th>Total Fat (g/d)</th>
<th>Linoleic Acid (g/d)</th>
<th>α-Linolenic Acid (g/d)</th>
<th>Protein (g/d)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infants</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-6 mo</td>
<td>0.7*</td>
<td>60*</td>
<td>ND</td>
<td>21*</td>
<td>4.4*</td>
</tr>
<tr>
<td>7-12 mo</td>
<td>0.8*</td>
<td>95*</td>
<td>ND</td>
<td>20*</td>
<td>4.6*</td>
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<tr>
<td><strong>Children</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1-3 y</td>
<td>1.3*</td>
<td>130</td>
<td>19*</td>
<td>ND</td>
<td>7*</td>
</tr>
<tr>
<td>4-8 y</td>
<td>1.7*</td>
<td>130</td>
<td>25*</td>
<td>ND</td>
<td>10*</td>
</tr>
<tr>
<td><strong>Males</strong></td>
<td></td>
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<tr>
<td>9-13 y</td>
<td>2.4*</td>
<td>130</td>
<td>31*</td>
<td>ND</td>
<td>12*</td>
</tr>
<tr>
<td>14-18 y</td>
<td>3.3*</td>
<td>130</td>
<td>38*</td>
<td>ND</td>
<td>16*</td>
</tr>
<tr>
<td>19-30 y</td>
<td>3.7*</td>
<td>130</td>
<td>38*</td>
<td>ND</td>
<td>17*</td>
</tr>
<tr>
<td>31-50 y</td>
<td>3.7*</td>
<td>130</td>
<td>38*</td>
<td>ND</td>
<td>17*</td>
</tr>
<tr>
<td>51-70 y</td>
<td>3.7*</td>
<td>130</td>
<td>30*</td>
<td>ND</td>
<td>14*</td>
</tr>
<tr>
<td>&gt; 70 y</td>
<td>3.7*</td>
<td>130</td>
<td>30*</td>
<td>ND</td>
<td>14*</td>
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<td><strong>Females</strong></td>
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<tr>
<td>9-13 y</td>
<td>2.1*</td>
<td>130</td>
<td>26*</td>
<td>ND</td>
<td>10*</td>
</tr>
<tr>
<td>14-18 y</td>
<td>2.3*</td>
<td>130</td>
<td>26*</td>
<td>ND</td>
<td>11*</td>
</tr>
<tr>
<td>19-30 y</td>
<td>2.7*</td>
<td>130</td>
<td>25*</td>
<td>ND</td>
<td>12*</td>
</tr>
<tr>
<td>31-50 y</td>
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<td>25*</td>
<td>ND</td>
<td>12*</td>
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<td>2.7*</td>
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<td>ND</td>
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<tr>
<td>&gt; 70 y</td>
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<td>21*</td>
<td>ND</td>
<td>11*</td>
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<td><strong>Pregnancy</strong></td>
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<tr>
<td>14-18 y</td>
<td>3.0*</td>
<td>175</td>
<td>28*</td>
<td>ND</td>
<td>13*</td>
</tr>
<tr>
<td>19-30 y</td>
<td>3.0*</td>
<td>175</td>
<td>28*</td>
<td>ND</td>
<td>13*</td>
</tr>
<tr>
<td>31-50 y</td>
<td>3.0*</td>
<td>175</td>
<td>28*</td>
<td>ND</td>
<td>13*</td>
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<tr>
<td>14-18 y</td>
<td>3.8*</td>
<td>210</td>
<td>29*</td>
<td>ND</td>
<td>13*</td>
</tr>
<tr>
<td>19-30 y</td>
<td>3.8*</td>
<td>210</td>
<td>29*</td>
<td>ND</td>
<td>13*</td>
</tr>
<tr>
<td>31-50 y</td>
<td>3.8*</td>
<td>210</td>
<td>29*</td>
<td>ND</td>
<td>13*</td>
</tr>
</tbody>
</table>

**NOTE:** The table presents Recommended Dietary Allowances (RDAs) in bold type and Adequate Intakes (AIs) in ordinary type, followed by an asterisk (*). RDAs and AIs may both be used as goals for individual intake. RDAs are set to meet the needs of almost all (97 to 98 percent) individuals in a group. For healthy infants fed human milk, the AI is the mean intake. The AI for other life stage and gender groups is believed to cover the needs of all individuals in the group, but lack of data or uncertainty in the data prevents being able to specify with confidence the percentage of individuals covered by this intake.

*Based on 0.8 g/kg body weight for the reference body weight.

*Change from 13.5 in prepublication copy due to calculation error.

#### Dietary Reference Intakes (DRIs): Additional Macronutrient Recommendations

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<thead>
<tr>
<th>Macronutrient</th>
<th>Recommendation</th>
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<tr>
<td>Dietary cholesterol</td>
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</tr>
<tr>
<td>Trans fatty acids</td>
<td>As low as possible while consuming a nutritionally adequate diet</td>
</tr>
<tr>
<td>Saturated fatty acids</td>
<td>As low as possible while consuming a nutritionally adequate diet</td>
</tr>
<tr>
<td>Added sugars</td>
<td>Limit to no more than 25% of total energy</td>
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