

Association between sleep disorders, obesity, and exercise: a review

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Abstract: Decreased sleep duration and quality is associated with an increase in body weight and adiposity. Insomnia, obstructive sleep apnea, and restless legs syndrome are three of the most prevalent types of sleep disorder that lead to an increased risk for numerous chronic health conditions. Various studies have examined the impact of these sleep disorders on obesity, and are an important link in understanding the relationship between sleep disorders and chronic disease. Physical activity and exercise are important prognostic tools in obesity and chronic disease, and numerous studies have explored the relationship between obesity, sleep disorders, and exercise. As such, this review will examine the relationship between sleep disorders and obesity. In addition, how sleep disorders may impact the exercise response and how exercise may impact patient outcomes with regard to sleep disorders will also be reviewed.

Keywords: obesity, sleep disorders, obstructive sleep apnea, insomnia

Introduction

The International Classification of Sleep Disorders currently lists more than 80 distinct sleep disorders (SD) divided into eight categories, including insomnia, sleep disordered breathing (SDB), and sleep-related movement disorders.¹ SD occur in a large proportion of the adult population, with 10%–13% of adults estimated to suffer from chronic insomnia and an additional 25%–35% having occasional insomnia.² Obstructive sleep apnea (OSA), the most prevalent form of SDB, has been estimated to occur in approximately 2%–4% of adults.³ It is further estimated, however, that a large proportion of individuals (93% of women and 82% of men) with clinically significant OSA remain undiagnosed, suggesting a much larger overall prevalence rate.⁴ Restless legs syndrome (RLS) is a prevalent form of sleep-related movement disorder with prevalence estimates ranging between 4% and 29%.⁵ These disorders all result in decreased sleep duration and quality, which has been associated with increases in body weight and adiposity.^{6,7} In OSA alone, it has recently been estimated that in those with a body mass index (BMI) of 25–28 kg/m² (overweight classification), prevalence rates increase to 20% and 7% for mild and moderate to severe OSA, respectively.⁸

The relationship between SD and obesity is likely an important mediating factor in the emerging research linking SD and other chronic disease, including cardiovascular disease (CVD) and diabetes mellitus, across all age groups.^{9–12} Understanding this link may increase the chances for the development of effective treatment interventions for both SD and obesity. A well-known treatment intervention for obesity is regular physical activity/exercise, which has recently begun to be investigated in relation to SD as well. Recent evidence, which will be reviewed within this manuscript, has

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suggested that the presence of a SD may impact the response to physical activity/exercise, be it acutely or chronically. This may have implications as to the effectiveness of physical activity/exercise as an intervention, but it may also aid in serving as a prognostic tool for the identification of those at increased risk for SD or other chronic conditions. Thus, this review will examine (1) the relationship between obesity and sleep disorders (ie, insomnia, OSA, and RLS); (2) the pathophysiological mechanisms linking these SD to obesity; and (3) the potential impact of these SD on physical activity and exercise, a primary intervention in addressing increased adiposity and obesity. Further, this review will focus on, but not be limited to, the previous 10 years (January 2002 to December 2012).

Insomnia

Diagnostic criteria for insomnia consists of symptoms relating to sleep disturbance, including difficulty initiating sleep, difficulty maintaining sleep, awakening too early, or sleep that is poor in quality in the presence of adequate opportunity and appropriate circumstances for sleep.¹³ Diagnosis of insomnia, unlike many other SD, is based on self-reported, and therefore subjective, sleep behaviors and sleep diaries completed by patients.¹⁴

The predominant theory regarding the pathophysiology of primary insomnia centers around a state of hyperarousal, manifested in hyperactivity of corticotropin-releasing factor (CRF).^{2,14,15} Initial insomnia may occur as a result of some psychosocial stressor or other precipitating factor that increases arousal of the hypothalamic–pituitary–adrenal axis.¹⁴ A study of young patients with insomnia, compared to age- and BMI-matched healthy controls, revealed higher 24-hour mean secretions of adrenocorticotrophic hormone and cortisol.¹⁶ Levels were markedly higher in patients with insomnia in the afternoon, evening, and early night measurements. Interestingly, the increase in 24-hour secretion did not appear to come from increased magnitude of pulsatile releases, but rather from increased concentrations during the “valley” periods of the 24-hour pulsatile profile and from an increased number of adrenocorticotrophic hormone and cortisol pulsatile releases. Additionally, hyperactivity of the regions of the brain responsible for wake promotion was supported by studies that utilized positron emission tomography scans to map glucose metabolism during wakefulness and non-REM sleep, and that this increase in glucose metabolism was associated with the number of times persons with primary insomnia awoke during the night.^{17,18}

Insomnia and obesity

Previous studies have indicated that persons with obesity are significantly more likely to report insomnia or difficulty with sleep.¹⁹ Additionally, over an average 7.5-year follow-up, persons with obesity were significantly more likely to develop chronic insomnia, although this effect was partially negated when controlling for sociodemographic and behavioral factors.²⁰ Finally, in persons with obesity, complaints of chronic emotional stress or sleep disturbance have been reported to be predictors for short sleep duration, rather than voluntary sleep curtailment as previously thought.²¹ Vgontzas et al further showed that in persons with obesity and without sleep disturbances or emotional stress, sleep duration was similar to non-obese control subjects.²¹ This may indicate the importance of detection and treatment of sleep disturbances as a potential therapeutic intervention for obesity.²¹

Insomnia, or its underlying pathophysiology, may play a role in predisposing one to overconsumption of energy, thus leading to weight gain. In a study of over 1000 volunteers from the Wisconsin Sleep Cohort Study, Taheri et al found that shorter sleep durations (5 hours per night versus 8 hours per night) were associated with 15.5% lower leptin levels and 14.9% higher ghrelin levels, independent of BMI, which may indicate that chronically shortened sleep duration could increase appetite, leading to overconsumption.²² Additionally, Dallman et al have proposed that chronic elevation of glucocorticoids, such as cortisol, similar to the proposed mechanism for insomnia, may play a role in increasing a person's desire to consume high fat and high sugar foods, as well as their propensity to store fat in the abdominal region.²³ They proposed that the chronically elevated levels of glucocorticoid hormones increase CRF activity in the central nucleus of the amygdala, increase stimulus salience, and increase abdominal obesity, which then serves as a means of increasing the metabolic inhibitory feedback on the catecholamines in the brain and CRF expression. This would indicate that the same pathway associated with hyperactivity in insomnia may promote the overconsumption of high fat and high sugar foods, as well as the deposition of abdominal fat stores, in an attempt to calm the hyperactivity occurring in the brain.²³

Insomnia and physical activity and exercise

Experimental evidence has suggested that exercise may be associated with better sleep quality.^{24–27} Although not specific to those diagnosed with insomnia, these studies have suggested that, in those with sleep difficulties, exercise may be effective at improving sleep outcomes, although this

remains unclear. Cross-sectional data has shown that physical inactivity has consistently arisen as a factor that increases one's likelihood for reporting symptoms of insomnia or poor sleep, even after controlling for other factors believed to affect insomnia risk.^{28–31} Further, it has recently been reported that maximal aerobic capacity was lower in those diagnosed with insomnia compared to those without insomnia, independent of other factors like age and sex.³²

In regards to exercise training with insomnia, an acute bout of moderate-intensity aerobic exercise approximately 3 hours before bedtime has been shown to reduce sleep onset latency, total wake time, and pre-sleep anxiety, while increasing total sleep time and sleep efficiency in those diagnosed with insomnia.³³ High-intensity aerobic exercise and moderate-intensity resistance training did not confer the same benefits. In older adults, a 16-week moderate intensity aerobic training program, with sleep hygiene education, was shown to improve self-reported sleep quality, mood, and quality of life versus sleep hygiene education alone.³⁴ The effects in this study were reported to be comparable to other reported cognitive behavioral interventions.^{35,36}

Obstructive sleep apnea

The pathophysiologic mechanisms of OSA are complex and compelling. Population based studies demonstrate a strong relationship between OSA and obesity – over 70% of individuals with OSA are considered clinically obese based on BMI status³⁷ – in addition to chronic diseases including hypertension, type 2 diabetes mellitus, CVD, and stroke.^{12,38} The link between OSA and obesity has been clearly documented with weight change impacting the Apnea-Hypopnea Index (AHI), a measure of OSA severity. In another analysis from the Wisconsin Sleep Cohort Study, which used a sample of 700 subjects, a 10% weight gain predicted a 32% increase in AHI score; conversely a 10% weight loss predicted a 26% decrease in AHI score over a 4-year period.³⁹ The strong relationship between OSA and obesity was replicated in the Sleep Heart Health Study and the Cleveland Family Study.^{40,41} Considerable research has demonstrated the reduction of OSA and related symptoms, including excessive daytime sleepiness, with weight loss, induced by diet and/or physical activity behavior change, medication, or through bariatric surgery.^{42–44}

OSA and obesity

Knowledge of the underlying connection with OSA and obesity is evolving and involves a two-way relationship affecting both the contribution of obesity to OSA and the implications of OSA contributing to obesity. Obesity contributes to the

development and severity of OSA through influences on the upper airway involving both respiratory neuromuscular control, and adipokine production. Independently, obesity appears to affect control of the upper airway through several mechanisms, including alterations in upper airway structure and function, reductions in resting load volume, and negative effects on respiratory drive and load compensation.⁴⁵ Additionally, neuromuscular control of the upper airway is negatively impacted by alterations in several key cytokines related to obesity, including leptin, tumor necrosis factor- α , and interleukin-6.⁴⁶ Independently, leptin can inhibit respiratory drive and OSA has been correlated with increased leptin levels.⁴⁷ Insulin resistance is also associated with OSA severity, independent of body weight, and may be linked with sleep deprivation or sympathetic activation.⁸ Location of fat deposition, specifically in the neck and viscera, can also contribute to OSA susceptibility.⁴²

The role of OSA contributing to obesity is less direct than the impact of obesity on the pathophysiology of OSA. Nonetheless, it is important to consider the contribution of OSA to obesity, thus potentially exacerbating obesity's impact on OSA. As described by Ong et al,⁴⁵ OSA impacts energy expenditure and caloric intake and thus overall body weight in a variety of ways, including: (1) changes in energy expenditure during times of sleep and wakefulness; (2) increased preference for energy dense food and increased caloric intake; (3) alteration in hormonal regulation specific to appetite and satiety; and (4) changes in sleep duration, which may decrease physical activity that is attributable to lethargy and daytime sleepiness.

Several studies have shown an increased preference for calorie dense foods, specifically fats and carbohydrates, in patients with OSA, independent from obesity.^{45,48,49} This preference may be tied to sleep fragmentation but has not been clearly elucidated.⁴⁶ Leptin and ghrelin are the key hormones related to appetite control. Increased leptin, to a state of leptin resistance, has been noted in obesity and as mentioned previously, increased leptin is associated with OSA status.⁴⁷

Obesity is a strong risk factor influencing OSA development, maintenance, and severity. Continued understanding of the mechanisms underpinning this relationship are critical to help determine appropriate treatment options. Weight reduction through various means continues to be viewed as a viable option to ameliorate OSA and related symptoms and thus potentially favorably impact associated chronic diseases. Additional research is warranted to determine the overall efficacy of weight reduction treatment modalities with long-term success.

OSA and physical activity and exercise

A physically active lifestyle can provide important health benefits for individuals with OSA. Importantly, regular exercise is associated with reductions in blood pressure^{51–54} and in the prevention of CVD^{41,55,56} – two of the most serious comorbidities associated with OSA.⁵⁷ Unfortunately, the salient clinical features of OSA suggest that patients are often disinclined or unable to initiate or maintain a regular exercise program. The sleep fragmentation of OSA frequently leads to excessive daytime sleepiness and lack of physical vigor. Furthermore, obesity is present in over 70% of patients,⁵⁸ and is implicated in both the development and progression of OSA.⁴¹ Although weight loss has been shown to decrease the severity of OSA, recent evidence suggests a bidirectional relationship between OSA and obesity, such that OSA also may promote weight gain and obesity.^{59,60} These findings present unique challenges for patients, and may partly explain why patients with OSA have difficulty losing weight.

The means by which effective and permanent weight loss is achieved is of growing importance to physicians treating patients with OSA. When used effectively, continuous positive airway pressure (CPAP) therapy is beneficial and has been shown to improve several adverse outcomes of OSA. Unfortunately, adherence levels are often suboptimal, particularly for patients with mild to moderate OSA⁶¹ and poor adherence often precludes important health benefits that otherwise may be associated with treatment. Furthermore, weight loss is not a consistent finding among obese OSA patients effectively treated with CPAP⁶² and preliminary evidence suggests that physical activity levels are not improved with CPAP, despite reductions in daytime drowsiness.⁶³ In this regard, encouraging patients to become more physically active may help break the cycle of weight gain and progression of OSA.

Exercise cardiopulmonary response characteristics in OSA

The majority of research to date on exercise in OSA has utilized graded exercise testing to help characterize the nature of cardiopulmonary stress attendant to this disorder, as well as to better understand functional abnormalities associated with OSA. These studies have demonstrated several distinct exercise response characteristics in OSA, including chronotropic incompetence,^{64–67} exaggerated blood pressure,^{65,66,68} and delayed heart rate recovery.^{69–71} Some studies also report that VO_2 peak is reduced in OSA.^{64,72–76} However, this is not a consistent finding, as others have reported no differences in exercise capacity between untreated patients with OSA and matched counterparts without OSA.^{65,69–71,77,78} Several

mediating factors may partly explain why some studies have found that OSA is associated with a reduced functional capacity, including OSA disease severity,⁷⁷ impaired muscle metabolism,^{76,79} reduced habitual daily physical activity secondary to daytime sleepiness,^{68,71,73,74,77} and cardiac dysfunction.^{78,80} Clearly, additional randomized controlled studies are needed to better understand the hemodynamic and pulmonary response characteristics in OSA. However, these studies lend preliminary support to the notion that OSA is associated with unique physiological response patterns during exercise, which may partially explain self-reports by patients that sustained exercise is unusually fatiguing.

Exercise training in OSA

Increasing interest has been generated in recent years concerning the potential benefits of exercise as an adjunct to primary treatment with CPAP. Since regular aerobic exercise is associated with body weight maintenance and, at higher volumes, weight loss,⁸¹ recommendations for increased physical activity frequently accompany primary treatment with CPAP⁸² and may be a viable means to increase daily energy expenditure and reduce secondary risk factors in OSA. In this regard, combining both exercise and weight loss with CPAP may provide the most effective treatment for many patients with OSA.

Few studies have examined the effects of exercise training on measures of OSA disease severity or other key clinical outcome measures in patients with OSA. Furthermore, a review of the published literature reveals that many of the previous studies that evaluated the efficacy of exercise training in OSA are limited by relatively small sample sizes^{83–87} that oftentimes lacked control groups.^{85–87} Moreover, several notable methodological differences exist between the majority of exercise training studies in OSA that complicate meaningful comparisons, including OSA sample population, disease severity, exercise testing protocols (exercise modes and test end points), and exercise training dose. Despite these limitations, preliminary evidence is encouraging and suggests that exercise training may be associated with reductions in OSA disease severity,^{86–89} improved exercise capacity,^{69,83,84,86} as well as improvements in daytime sleepiness, quality of life, and mood state.^{84,86,90} Although it seems likely that weight loss secondary to exercise training is the most likely mechanism for improvement in OSA disease severity, exercise alone has been shown to improve OSA severity even without significant weight loss.^{83,87–89}

Despite the lack of evidence to support specific exercise recommendations in OSA, it is reassuring that regular physical activity appears to be associated with higher

vitality, increased physical vigor, and reduced fatigue in patients with OSA.⁹¹ Epidemiological research also suggests a modest association between higher volumes of exercise and reduced severity of OSA that is independent of body habitus.⁹² Furthermore, data from the Sleep Heart Health Study demonstrate that vigorous exercise performed for at least 3 hours each week is associated with decreased odds of developing OSA.⁹³

Additional research is needed on the potential benefits of exercise in treating OSA. However, the results from these studies are encouraging and suggest that a physically active lifestyle may have long-term potential to forestall or even reverse the symptoms associated with OSA, and possibly prevent the development of OSA altogether. Furthermore, that the majority of these changes appear soon after initiation of CPAP therapy suggests that there is good potential to increase aerobic physical activity shortly after therapy has begun.

Restless legs syndrome

RLS is a disorder characterized by the irresistible urge to move the legs in response to a “creeping or crawly” sensation in the legs.⁹⁴ The sensation in the legs can be as severe as pain and is temporarily relieved by movement.⁹⁴ The impact of RLS on the individual can be profound and debilitating. RLS is associated with reductions in quality of life – reductions that are comparable to Parkinson’s disease and other chronic diseases.⁹⁵ RLS can negatively impact daily activities, where prolonged activities like sitting at a desk or riding in a vehicle can be difficult to impossible.⁹⁶ RLS is associated with delayed sleep onset, difficulty maintaining sleep, decreased total sleep time, and reduced or no slow-wave sleep.⁹⁷ Individuals with RLS are at increased risk for psychological disorders like panic disorder, generalized anxiety disorder, and depression.⁹⁸ In addition, RLS has demonstrated a positive relationship to increased CVD incidence, independent of confounding factors like age, sex, BMI, other sleep disorders, and lifestyle factors.⁵

The pathophysiological mechanisms of RLS are not well understood. The primary causes of RLS are believed to be dopaminergic and iron metabolism dysfunction,^{94,99–104} although this may only be a partial explanation.¹⁰⁵ Iron deficiency is not common in all RLS sufferers, and iron supplementation and dopaminergic agents have shown variable success in RLS treatment.⁵

RLS and obesity

Several studies across different countries have examined the relationship between RLS and obesity, most being cross-

sectional in nature. As a result, assessing the causal nature between the two is difficult. A majority of studies, however, do show a small yet significant relationship between RLS and obesity.^{106–113} This relationship has been demonstrated through a significantly greater BMI in those with RLS versus those without,^{107,113} an increased prevalence of RLS in obese versus nonobese individuals,^{109,110,112} or an increased prevalence of obesity in RLS versus non-RLS.^{106,111} These studies all adjusted for common confounding variables such as age, sex, and lifestyle factors (caffeine or alcohol consumption, smoking, physical activity).

The strength of the relationship between RLS and obesity, however, is open to interpretation. For instance, Schlesinger et al¹¹³ reported mean \pm standard deviation BMI values of 27.3 ± 0.3 and 26.5 ± 0.3 for RLS and non-RLS, respectively ($P = 0.003$). Elwood et al¹⁰⁷ reported similar mean values in their study (27.5 vs 26.6 for RLS vs non-RLS, $P < 0.001$). While statistically significant, the mean differences reported are small. In contrast, reported prevalence data may suggest a stronger relationship. Mustafa et al¹¹² reported that the prevalence of RLS was significantly higher in obese subjects (23%) versus nonobese subjects (16.4%). When comparing men with RLS versus those without, Mallon et al¹⁰⁶ reported an obesity prevalence (BMI ≥ 30 kg/m²) of 7.2% and 4.3%, respectively ($P = 0.05$). In women, the prevalence of obesity was 9.4% and 5.2% in RLS and non-RLS, respectively ($P = 0.01$).

RLS and physical activity and exercise

To date, very few studies have examined the impact of RLS on physical activity or exercise. One epidemiological study in over 1800 subjects reported that a lack of exercise (<3 hours per month vs ≥ 3 hours per month) was associated with an increased risk of RLS (odds ratio = 3.32).¹¹⁴ A recent study by Daniele et al¹¹⁵ examined the physical activity habits of RLS patients and found that while RLS severity did not differ across physical activity levels assessed by questionnaire, more active RLS patients reported greater quality of life variables, suggesting the potential value of physical activity in RLS patients.

Exercise training in RLS

Only two recent studies were identified that have examined the impact of exercise training on RLS. Esteves et al¹¹⁶ trained eleven RLS subjects at their anaerobic ventilatory threshold for 72 sessions (approximately 6 months) and found that subjective symptoms of RLS were significantly improved after training.

One randomized controlled trial has been conducted in RLS patients.¹¹⁷ In this study, 41 subjects were randomized to either an exercise or non-exercise group. The exercise group performed aerobic and lower extremity resistance training 3 days per week for 12 weeks. Similar to the previous study, RLS symptoms were significantly improved following the training period (total severity score 20.6 vs 12.1 for baseline and 12 weeks, respectively) whereas the control group did not change (22.5 vs 21.5). These findings suggest that physical activity and/or exercise may have a significant positive impact on the quality of life of RLS sufferers, and may aid in improving the obesity status of those with RLS.

Summary and future directions

Sleep disturbances and sleep deprivation, whether caused by insomnia, SDB, or a sleep-related movement disorder, does appear to have a relationship with development of or exacerbation of body adiposity or vice versa. The nature of the published research, predominantly cross-sectional and observational in nature, makes it difficult to ascertain clearly whether it is the SD contributing to obesity, or obesity contributing to the SD. More research, with large sample sizes and controlled for confounding factors are needed. It is most likely a combination of both, each contributing to a downward spiral of worsening sleep habits and body adiposity. In all three cases discussed within this review (insomnia, OSA, RLS) however, evidence does exist suggesting that the presence of a SD may increase the risk for obesity.

There does, however, appear to be a positive influence of exercise in SD. In all three cases, quality of life and/or severity outcomes appear to be positively impacted by regular exercise. Adopting a physically active lifestyle may be a key intervention for the treatment of SD and obesity, and may be a long-term solution to improved quality of life and decreased risk for the chronic conditions associated with these SD. Further research is needed with long-term randomized controlled trials to best elucidate this relationship.

Disclosure

The authors report no conflict of interest in this work.

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