REVIEW ARTICLE

Association between Sleep – disordered breathing and obesity

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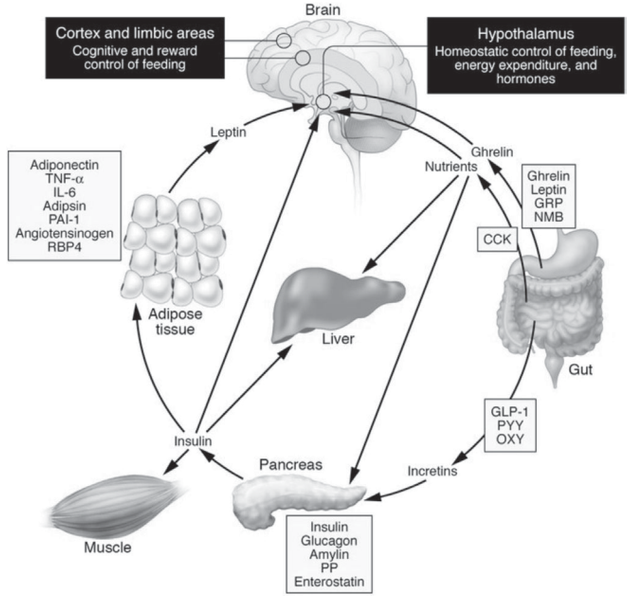
Introduction

Obesity has reached epidemic proportions in India in the 21st century with morbid obesity affecting 5% of the countries population.(1) Although currently defined by the WHO (World Health Organization) in terms of excess weight for a given height (2) obesity is best considered as being an increase in adiposity. It is interesting to note that along with obesity, sleep disordered breathing (SDB) are on rise. Using data from 690 adults in the Wisconsin sleep cohort study Peppard et al. (3) found that a 10% weight loss was associated with 26% decrease in AHI (Apnea and Hypopnea Index). Thus weight gain of 10% was associated with a 6 fold increase in the odds of developing moderate to severe SDB. Because of this and other similar findings, there has been considerable interest in treating SDB using a range of obesity interventions such as dietary changes, behavioral modification, and for selected patient's bariatric surgery. Unfortunately the success of these interventions has been inconsistent. This inconsistency triggers a thought that SDB may be associated with alteration in energy metabolism that, in turn, leads to weight gain and complicate the treatment of these two disorders that often coexist.

Obesity and leptin

According to the First Law of Thermodynamics, obesity results from an imbalance between energy expenditure and energy intake culminating in excessive accumulation of fat in adipose tissue, liver, muscle, pancreatic islets, and other organs involved in metabolism (4). Our knowledge of the neurobiology of feeding and energy homeostasis has benefited from the discovery of fat and gut derived hormones and their target in the hypothalamus. (5) Fig-1.

Leptin is secreted by fat cells (adipocytes) and was originally thought to signal to the brain to inhibit food intake and decrease weight (5, 7). This concept was partly driven by the observation that humans and rodents lacking in functional leptin protein or receptor manifested vigorous feeding and obesity (5). As was predicted, leptin treatments particularly direct injection of leptin into the cerebral ventricle or hypothalamus, profoundly inhibited food intake and decreased weight and fat in animals



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lacking leptin (5, 6, 7). However, the notion of leptin as an anti-obesity hormone was called into questions because obesity is typically associated with high leptin levels not leptin deficiency. Moreover, rodents and humans that become obese on a high fat (Western) diet do not respond to leptin (8). Studies have demonstrated that leptin is transported into the brain, binds to its receptor in the hypothalamus, and activates JAK-STAT3, leading to suppression of "orexigenic peptide" (e.g. neuropeptide Y and or goute-related protein which normally increase food intake), and increase in "anorxigenic peptides" (e.g. proopiomelanocortin and corticotrophin-releasing hormone) which normally decrease food intake. (6, 7, 8).

Sleep-disordered breathing and hormones with special reference to leptin

Sleep-disordered breathing (SDB) is an extremely common condition that compromises the vital functions of respiration and circulation producing a myriad of adaptive physiological acid-base disbalance. Therefore. SDB has wide spread systemic effects, which are unfortunately, rarely considered by medical professionals other than those specialized in diagnosing and treating this disorder. The many adaptive endocrine alterations associated with SDB are an example of how a seemingly local upper airway dysfunction induces systemic consequences, affecting every cell of the organism. Conversely, manifestation of sleep apnoea is critically linked with control of breathing. All endocrine changes that increase the tendency for periodic breathing will also increase the episodes of sleep apnoea. The present review focuses on SDB secondary to leptin and its effect on obesity.

The concept of SDB has markedly evolved during the past decade. The episodes of sleep apnoea and hypnoea result from periodic total or partial closure of the upper airway. These episodes are often accompanied by hypoxaemia and terminated with cortical electroencephalogram arousals. The severity of SDB is commonly expressed as the apnoea/hypopnoea index (AHI), which indicates the frequency of the apnoea/ hypopnoea episodes per hour of sleep. Some authors also include the respiratory effort-related arousals and express the severity of SDB as the respiratory disturbance index (RDI).

Sleep apnoea seems like an epidemic, which spreads rapidly with obesity, another major health problem in Western societies and Western aping societies. A number of hormones interacts with sleep (9) and breathing (10). SDB affects hormones via a number of mechanisms. Conversely, hormones and endocrine states induce, aggravate or alleviate SDB. Finally, nasal continuous positive airway pressure (CPAP) therapy influences hormone secretion.

SDB and sleep disturbances interact with hormones in several ways. Episodes of apnoea or hypopnoea cause sleep fragmentation and disturb sleep cycles and stages. Arousals induce stress response resulting in increased levels of stress hormones (11). Hypoxia may also have a direct effect on central neurotransmitters,(12) which result in alterations in the hypothalamo-pituitary axis and in secretion of the peripheral endocrine glands (13), Hypercapnia alone or combined with hypoxia may increase levels of renin, adrenocortiocotrophic hormone, corticosteroids, aldosterone and vasopressin (13,14). Finally, disorganization of sleep, sleep loss and naps disturb sleep-controlled endocrine rhythms resulting in endocrine and metabolic abnormalities.

Leptin, besides its best known function as a satiety hormone, is also a powerful respiratory stimulant (15). Plasma leptin levels are higher in sleep apnoeics than in controls matched for BMI (16). Furthermore, hypercapnic patients with obstructive sleep apnoea syndrome (OSAS) have higher leptin levels than eucapnic BMI-matched controls with sleep apnoea (17). Leptin secretion could provide an adaptive mechanism to enhance ventilation in patients with severe respiratory impairment at the level of the central nervous system. Elevated leptin levels are likely to contribute to the comorbidity of OSAS because high leptin levels are associated with coronary heart disease (18), insulin resistance (19), impaired fibrinolysis (20), development of obesity (21) or type-2 diabetes, all of which are highly prevalent in patients with OSAS.

Conclusion

Obesity and sleep disordered breathing has acquired the shape of an epidemic in developing and developed countries. Though sleep disorder breathing is still under diagnosed, obesity, a physical change is diagnosed early. Contrary to the belief that obesity leads to SDB, increased leptin level in SDB which leads to leptin resistance could be an isolated factor for obesity.

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