Obstructive sleep apnea (OSA) is a common disorder, characterized by recurrent episodes of apnea or hypopnea secondary to complete or partial upper airway obstruction, leading to significant adverse health consequences. The pathogenesis of obstructive sleep apnea is due to the interaction between anatomic upper airway susceptibility and sleep-related changes in upper airway function. The loss of the “wakefulness drive to breathe” results in decreased caliber of the pharyngeal lumen, increased upper airway resistance, and increased compliance of the upper airway wall.

Extensive research has focused on the neuromuscular determinants of upper airway patency, especially the genioglossus muscle and the hypoglossal motoneurons, and the effect of lung volume and tracheal traction on upper airway patency. However, available studies have not provided a satisfactory answer to a very simple question: what is the link between obesity and upper airway obstruction?

In this issue of SLEEP, Brennick and colleagues provide a direct link between obesity and compromised upper airway lumen. The investigators examined the effects of obesity on upper airway structures in obese (OBZ) and lean (NBZ) Zucker rats, assessing tongue fat and volume using in-vivo magnetic resonance spectroscopy (MRS), MRI including Dixon imaging for tongue fat volume, ex-vivo biochemistry, and histology. The investigators found a large degree of fat infiltration in the tongue muscle in genetically obese Zucker rats, as compared to tongues of the nonobese Zucker rats. Interestingly, fat accumulated primarily in the tongue and not in other upper airway skeletal muscle. The volume of the OBZ tongue was not greater than the NBZ tongue. However, total fat volume measured by MR fat weighted Dixon image analysis was significantly greater in OBZ tongues.

The susceptibility to fat deposition in the tongue may have significant implications for the pathogenesis of OSA. Excessive lingual fat deposits may increase collapsing tissue pressure and promote pharyngeal narrowing. The findings of Brennick et al. corroborate studies in humans that demonstrated greater fat deposits in sleep apnea antero-lateral to the upper airway in patients with OSA when compared to control participants. Similarly, mass loading in anesthetized rabbits, simulating excessive adipose tissue, was found to be associated with increased upper airway resistance and collapsibility, elevating compressive tissue pressure surrounding the upper airway, and subsequent pharyngeal narrowing.

The mechanical effect of lingual fat deposition may be influenced by the surrounding structures, especially the size of the mandible. While Brennick et al. were unable to demonstrate a difference in the volume of the tongue, the location of the fat deposits may lead to increased tissue pressure if the tongue is constrained by a small mandibular enclosure. Using MRI in patients with OSA, Shelton et al. demonstrated that the size of the region enclosed by the mandible was critically important to the genesis of OSA. Accordingly, fat depsoits in the upper airway and craniofacial abnormalities may have an additive or synergistic collapsing effect on the upper airway by elevating the upper airway surrounding tissue pressure.

Deposition of lingual fat represents a mechanical load that may impair the ability of the genioglossus to dilate the airway effectively. In awake goats, stimulation of the genioglossus results in fiber muscle shortening when the goats breathed through a tracheostomy tube, but fiber lengthening when the goats breathed through a resistive load. Fat infiltration may also affect the utility of hypoglossal electrical stimulation as a treatment of obstructive sleep apnea in obese individuals with large fat deposits and the efficacy of the surgical interventions that focus on the tongue base. Finally, increased lingual fat deposits, combined with the mechanical constraint of a small mandibular enclosure may provide a physiologic explanation for the noted correlation between ventilatory motor output and upper airway narrowing during periodic breathing or central apnea in “susceptible” individuals and may explain the occurrence of expiratory narrowing of the upper airway in patients with OSA.

The study by Brennick et al. poses a few unanswered questions. What are the determinants of lingual fat deposits? Is there a gender effect similar to the effect on neck circumference? What is the role of age or menopausal state on lingual fat deposits? It is also important to determine if these deposits are metabolically active. Does the presence of lingual fat correlate with visceral fat deposits or with the metabolic consequences of obesity?

An important question is whether decreased weight would reduce the size of lingual fat in humans. Studies involving weight loss have shown a salutary but variable effect on AHI. However, one prospective study demonstrated resolution of SDB in patients following gastric bypass in two-thirds of the patients who achieved a 30% decrease in weight. An important issue is whether the reported improvement is due to decreased lingual fat accumulation or other physiologic changes that accompany weight loss. Finally, identification of a
specific propensity may identify potential metabolic pathways to prevent such deposits and their adverse effects.

In conclusion, the relationship between obesity and lingual fat deposits is an exciting new finding. However, future studies in humans are needed to determine the occurrence and significance of lingual fat deposits in humans and whether they contribute to the pathogenesis of obstructive sleep apnea. Future studies in lean and obese humans and in humans undergoing gastric bypass for weight loss may help us determine whether this finding is an etiologic factor or an epiphenomenon.

**REFERENCES**


**DISCLOSURE STATEMENT**

Dr. Badr has indicated no financial conflicts of interest.

**REFERENCES**


