HIGHLIGHTED TOPIC | Upper Airway Control and Function: Implications for Sleep-Disordered Breathing

Biomechanical properties of the human upper airway and their effect on its behavior during breathing and in obstructive sleep apnea

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Bilston LE, Gandevia SC. Biomechanical properties of the human upper airway and their effect on its behavior during breathing and in obstructive sleep apnea. J Appl Physiol 116: 314–324, 2014. First published July 3, 2013; doi:10.1152/japplphysiol.00539.2013.—The upper airway is a complex, multifunctional, dynamic neuromechanical system. Its patency during breathing requires moment-to-moment coordination of neural and mechanical behavior and varies with posture. Failure to continuously recruit and coordinate dilator muscles to counterbalance the forces that act to close the airway results in hypopneas or apneas. Repeated failures lead to obstructive sleep apnea (OSA). Obesity and anatomical variations, such as retrognathia, increase the likelihood of upper airway collapse by altering the passive mechanical behavior of the upper airway. This behavior depends on the mechanical properties of each upper airway tissue in isolation, their geometrical arrangements, and their physiological interactions. Recent measurements of respiratory-related deformation of the airway wall have shown that there are different patterns of airway soft tissue movement during the respiratory cycle. In OSA patients, airway dilation appears less coordinated compared with that in healthy subjects (matched for body mass index). Intrinsic mechanical properties of airway tissues are altered in OSA patients, but the factors underlying these changes have yet to be elucidated. How neural drive to the airway dilators relates to the biomechanical behavior of the upper airway (movement and stiffness) is still poorly understood. Recent studies have highlighted that the biomechanical behavior of the upper airway cannot be simply predicted from electromyographic activity (electromyogram) of its muscles.

pharynx; biomechanics; starling resistor; genioglossus

DYNAMIC BEHAVIOR OF THE HUMAN UPPER AIRWAY

The human upper airway is a dynamic structure, the anatomy of which not only permits the respiratory functions that are the focus of this minireview, but also swallowing and speech. Its neural control and mechanical behavior are an evolutionary compromise between these demands (19). This neuromechanical “system” must respond rapidly and be dynamically controlled. The system changes during the respiratory cycle, between wakefulness and sleep, and between sleep stages.

At any moment, upper airway patency depends on a delicate dynamic balance between pressure in the upper airway and the dilatory forces in the heterogeneous soft tissues that surround it. If inward radial tissue stresses (the radial component of the stresses in the tissue wall1) around the airway exceed pressure within the airway, then narrowing (hypopnea) or occlusion (apnea) occurs. While multiple mechanisms can prevent such narrowing, a key feature of the upper airway is that small changes in intraluminal pressure, neural drive to the dilator muscles, or tissue mechanical properties can disturb this balance and lead to airway occlusion. From a mechanics standpoint, this is a “critically stable” system, one in which there is no guarantee that a perturbation of the system will not tip it into an unstable state (26).

There are both “passive” and “active” components to the mechanical behavior of the airway tissues. Passive components include the static size, composition, and shape of the airway and soft tissues, and they govern the predisposition to collapse. Active components derive from dynamic respiratory cycle-
related changes, and they include muscle activity produced by reflex and central drives and tissue deformation produced by changes in airway pressure. Active components can either increase or decrease the propensity of the airway to collapse. Also, the functional behavior of soft tissues surrounding the pharynx is influenced by the bony tissues to which they are connected, as the bony boundaries constrain movement of the soft tissues.

This minireview focuses on the mechanical characteristics and responses of the soft tissues in the human upper airway and considers some approaches that can characterize this behavior in health and disease.

MECHANICAL MODELS OF THE UPPER AIRWAY SYSTEM

The pharynx is often thought of as a “floppy tube” (Fig. 1A). Mechanical models of collapsible tubes, such as the Starling resistor, are used to relate airflow, intraluminal pressure, and peripharyngeal tissue pressures (e.g., Refs. 2, 34, 58, 74). These have provided insights into the mechanisms of flow limitation, which occurs when increasingly negative pressure at the epiglottis fails to increase airflow (33), and how additional peripharyngeal tissue pressure can encourage collapse (40, 41). Refinements to this concept include the compliance of the tube wall, which is not included in a “classical” Starling resistor. Increased tension in the airway wall from tracheal traction due to increased lung volume would reduce collapsibility, while decreases in tracheal traction due to decreased lung volume would promote collapse (e.g., Refs. 2, 73). However, models based on the Starling resistor have major limitations, as they largely ignore the contribution of the mechanical characteristics, muscle activity, and functional anatomy of the airway walls, not least of which is that parts of the pharynx (tongue, lateral walls, and soft palate) can behave independently, or can interact nonuniformly, and thus they do not form a uniform collapsible tube required in simplistic models.

Airway patency has long been understood to rely on a balance between airway pressure and muscle activity (5, 62), and this was conceptualized by Isono and colleagues (34) as having the airway balancing on a fulcrum representing the intrinsic mechanical behavior of the upper airway. They later proposed another conceptual model (Fig. 1B), balancing soft tissue and intramandibular volume (37) to explain how obesity (in those with “normal” craniofacial bony structure), head, neck, and jaw postures, or craniofacial variants that reduce the volume of the oral cavity and pharynx (bounded by the mandible, cervical spine, and hard palate) predispose the upper airway to collapse. For example, fat deposits in the pharynx increase the volume of the soft tissues and diminish the space for the airway within the “bony box.” This model also has limitations, as the bony box is bounded on only three sides, and the model does not explain why all of the excess soft tissues cannot be accommodated below the mandibular plane. Additional soft tissue is present below the mandibular plane, particularly in obstructive sleep apnea (OSA) patients and the obese (22, 64). Furthermore, this model cannot explain why some healthy obese individuals do not develop OSA, despite the same anatomical risk factors (including “crowding” of the upper airway) as OSA patients. Nor can the model fully account for changes in OSA severity with head position and mouth opening.

Aittokallio and colleagues (1) created a mathematical model of the upper airway in which the airway stiffness was allowed to vary along the length of the pharynx and during the respiratory cycle (representing muscle activity), while Longobardo and colleagues (47) modeled neurochemical and biomechanical factors in upper airway control in a compartmental model using the “tube law.” Oliven et al. (58) showed that airflow in the pharynx during electrical stimulation of the genioglossus and mandibular advancement can be predicted from a modified tube law model, provided that airway compliance, cross-sectional area, airway resistance, and pressure are measured. These complex models allow exploration of several interacting factors in ways that are difficult experimentally, but they suffer from lack of data on the realistic mechanical behavior of upper airway tissues and have many arbitrary parameters. This limits their predictive capacity.

More recently, there have been several more complex computational biomechanical models of the upper airway. Many are based on imaging data and thus have anatomically realistic geometries and may be either two or three dimensional. They
have tended to focus on either soft tissues (using finite-element techniques) or airflow (using computational fluid dynamics techniques), where the airway walls are modeled as rigid structures. New developments in fluid-structure interaction modeling should allow the airflow and tissue compliance to be simulated concurrently (e.g., Ref. 96). However, realistic models of muscle activity, mechanical properties of the tissues, and mechanical linkages between muscles are still needed. Such models may then allow insight into mechanisms of upper airway collapse and provide clearer understanding of the interactions between anatomy and mechanical behavior of the upper airway tissues.

The remainder of this review focuses on experimental measures of mechanical behavior of the soft tissues of the human upper airway and their influence on airway patency.

**Passive Characteristics of Upper Airway Tissues**

Like most soft biological tissues, those of the upper airway are mechanically complex, and their mechanical properties cannot be defined by a single numerical value for “stiffness,” even when passive. Moreover, the soft tissues of the upper airway are inhomogeneous, being made up of different tissues (muscle, fat, connective tissue) arranged in a complex geometry. The stiffness of these tissues depends on the mechanical properties of each component in isolation, as well as their anatomical arrangement (geometry), and their interaction across a range of physiological states.

**Tissue Mechanics and Effects of Structure**

In biomechanical terms, the passive stiffness of the upper airway tissue is defined by its response to an applied load or deformation, normalized by the area over which loading is applied. A familiar concept is the modulus of elasticity, or Young’s modulus (denoted \( E \)), which is the force per unit area (stress), divided by the change in length per unit length (strain) of the tissue (\( E = \frac{\text{stress}}{\text{strain}} \)). However, in upper airway tissues, the modulus of elasticity varies with the amount of load, the direction in which the load is applied (relative to the muscle fascicles), and the loading rate. As the applied load is increased, the instantaneous Young’s modulus (tangent of the stress/strain curve) increases (see Fig. 3). This is nonlinear elasticity. One consequence is that, when the tissues of the upper airway are slack, or nearly slack, small pressure changes produce large deformations of the airway walls, while airway tissues under load will deform much less in response to the same pressure change. In addition, under a constant force or pressure, the tissues will “creep” or deform over time. Similarly, if a constant stretch is applied, the tension (or stress) will decrease over time, as the tissue “relaxes,” although typically a residual stress remains. The speed at which a load is applied also affects the tissue response, with the tissue appearing “stiffer” at faster loading rates. These three behaviors are all characteristic of viscoelasticity of the tissue, which exhibits both elastic (solid) and viscous (fluid) characteristics. Muscles also exhibit “thixotropy,” which increases the apparent stiffness postcontraction, due to a proportion of cross bridges effectively remaining attached (e.g., Ref. 61). This has not been studied in upper airway muscles. Finally, muscle is stiffer along the direction of muscle fascicles than perpendicular to them, and so loads applied in different anatomical directions will result in different movements.

The tongue is often considered to be a “muscular hydrostat” (28), whereby complex arrangements of the muscle fibers and their activation, together with tissue incompressibility, give rise to deformation (Fig. 1C). While incompressibility of the tongue (i.e., the volume is constant) has not been convincingly demonstrated in the human in vivo, there is some support for this idea (e.g., Refs. 28, 80). This characteristic is common in hydrated soft tissues, as water is largely incompressible at physiological pressures, and fluid flow into and out of the tissue is typically slower than the loading. As a consequence, incompressibility means that, when the tongue is compressed anteroposteriorly, it must expand laterally, or vertically, or both.

Purely anatomical or geometric characteristics play a role in the biomechanical response of the upper airway soft tissues. For example, the longer pharynx of males has been proposed to explain increased rate of OSA in men compared with women (49, 75, 81). Two mechanical factors contribute. A longer structure is more flexible than a shorter structure with the same cross section, and, in a longer structure, the airway surface area is larger, so that the airway pressure is applied over this larger area, so the net force is also greater. Airway curvature and mucosal folding may also affect local collapsibility.

Measurement of the passive mechanical behavior of the upper airway is difficult, particularly in human subjects, as there is always some neural drive to the airway musculature, since all neural inputs cannot be removed in practice. Such measurements have been performed in animals [see the related minireview by Fregosi and Ludlow (26a)]. In humans paralyzed during general anesthesia (where the effect of neural drive is removed), both adult and pediatric sleep apneic subjects have more compliant upper airways than healthy subjects (34, 35). A common concept used to characterize airway collapsibility is the most negative (intraluminal) pressure that the airway can withstand before collapsing, with more negative “closing pressures” indicating a less collapsible airway. Adults with mild (5–20 events/h) or moderate to severe OSA (>20 events/h) had higher (i.e., less negative) pharyngeal closing pressures (0.90 ± 1.34 and 2.78 ± 2.78 cmH\(_2\)O, respectively) than age- and body mass index (BMI)-matched subjects (−3.77 ± 3.44 cmH\(_2\)O; \( P < 0.01 \)) (34). Children with sleep-disordered breathing had higher closing pressures (3.5 ± 4.3 cmH\(_2\)O) than healthy children (−7.4 ± 4.9 cmH\(_2\)O) (35). These data represent “net compliance” of the upper airway, and the relative contribution of intrinsic tissue mechanical properties and purely geometric factors to these differences is unclear. Measurements of the critical closing pressure (\( P_{\text{crit}} \)) in sleeping, nonparalyzed adults have also shown that the pharynxes of apneic subjects are more collapsible than those of nonapneic subjects (29), but ongoing muscle activity means that the pharynx is not passive, and short- and long-latency reflexes will operate during such experiments. Comparisons of the passive mechanical behavior of the upper airway during sleep and wakefulness are rare, as it is difficult to eliminate dynamic effects (e.g., by using muscle paralysis) during wakefulness. However, pharyngeal collapsibility appears to increase substantially during sleep based on the responses to brief negative-pressure pulses (50, 88). There is a moderately strong correlation between collapsibility when awake and asleep (50).
This shows that the intrinsic tissue mechanical behavior is a major contributor to collapsibility of the upper airway, irrespective of sleep-wake state.

Intrinsic Mechanical Properties of Upper Airway Tissues

Few mechanical tests of the tissues of the upper airway have been reported. Gerard et al. (27) performed indentation testing of a single human cadaver tongue, but similar studies comparing the biomechanics of OSA patient groups with healthy volunteers have not been performed. Myotonomometry is a technique used to measure skeletal muscle properties. The underlying physics principle is that the vibration response of a material varies with the viscoelastic properties of the material. This can be quantified from the vibration frequency in response to a “tap” on the tissue. Endopharyngeal myotonomometry indicated that the soft palate and tongue of OSA patients in vivo was stiffer than that of control subjects (83, 84). The viscous component, which is measured by how quickly the magnitude of the vibration decays due to damping by the tissue (incorrectly termed elasticity in the original articles), was not different between groups. Unfortunately, muscle activity was not controlled, and the groups were poorly matched for obesity, making these results difficult to interpret. The effect of increased fat on the mechanical properties of the tongue and adjacent soft tissues is not known. Mechanical testing of uvula tissue ex vivo (76) shows that tissue from apneic subjects required more force to be elongated than in snorers, but the measurements did not account for the cross-sectional area of the samples. As the muscularis uvulae was larger in apneic subjects, these conclusions are unreliable. It is also unclear whether tissue properties of the uvula can be generalized to other components of the upper airway.

Magnetic resonance (MR) elastography tracks the propagation of mechanical vibrations through tissues to measure tissue viscoelastic properties. The underlying physics principle is that vibration waves travel faster in stiffer materials and attenuate more rapidly in more viscous materials. By determining the speed of shear wave propagation and the decay of the vibration as it travels, using phase-contrast MRI to capture the displacements across a vibrating tissue, the elastic and viscous properties of the tissue can be obtained. MR elastography has been used to measure “average” properties of the tongue and soft palate over several minutes, in awake young volunteers, OSA patients, and age- and BMI-matched control subjects using a vibrating mouth guard as the source of vibration (6, 17). These studies show that the tongue and soft palate are very soft and are softer in OSA patients than in controls [OSA patients shear modulus 2.68 ± 0.35 kPa vs. age- and BMI-matched subjects 2.98 ± 0.44 kPa, P < 0.001, measured using 80-Hz vibration (7)]. Some typical data are shown in Fig. 2. The latter study suggested that the differences in the patients are directional, with reduced stiffness in the direction of the muscle fibers in the tongue implicating them in these changes. The ratio of the shear moduli, μ ⊥ parallel and perpendicular to the fiber direction in OSA patients was μ∥/μ⊥ = 0.95 ± 0.01 compared with control subjects μ∥/μ⊥ = 1.07 ± 0.15, P = 0.02. This remains to be confirmed in larger studies. Alterations in the tissue microstructure in OSA could underpin these observations. This explanation is supported by a recent microscopy study of surgical samples of palatopharyngeal muscle (53), which found that muscle-fiber diameter was smaller in OSA patients, and thus there was a relative increase in the volume of elastic and collagenous material. These changes were larger in more severe OSA patients. There was more amorphous material in the interstitial space in samples from OSA patients than control samples. Elastography was also used to show that the application of continuous positive airway pressure (CPAP) did not acutely change tissue stiffness (7), even though CPAP substantially reduces muscle activity (78). This suggests that the usual levels of active contraction contribute minimally to tissue stiffness under these conditions. Other studies of tongue mechanical properties confirm that the tongue and soft palate (including the overlying mucosa) are highly compliant tissues when passive, but do not compare tissue behavior in apneic subjects and controls (4, 27, 42).

Factors That Influence Upper Airway Tissue Mechanical Properties

Many factors affect passive mechanical behavior of upper airway tissues, but few have been well studied. Fat content may alter the passive tissue stiffness, but measurements of the effect of fat on muscle tissue passive mechanical properties in vivo are not available. While increased upper airway fat deposition is associated with increased OSA risk and higher Pcrit (e.g., Ref. 46), fat deposits also narrow the airway. Hence, separation of the contribution of fat to geometric and stiffness changes is difficult. MR elastography showed that OSA patients have a less stiff genioglossus than subjects of similar BMI when awake, when gross fat content in the tongue was not significantly different between the groups (7). However, that study did not quantify total tissue fat content or its distribution. Different patterns of upper airway fat deposition between men and women may also affect upper airway collapsibility and OSA prevalence (90). Increased tracheal traction, as occurs at elevated lung volumes, might increase the effective stiffness of the airway walls (49), and, conversely, airway stiffness may decrease at reduced lung volumes (31). In the rabbit, increased tracheal traction reduces collapsibility of the upper airway (39). Furthermore, increasing lung volume can reduce the severity of OSA (30) and/or reduce required CPAP pressures. The mechanisms are unclear. One possibility is that the upper airway wall tissues are stretched by elongation produced by the lung volume increase, thus shifting them from the “toe region” of their stress-strain curve into the stiffer region (Fig. 3B). Changes in lung volume due to male-pattern central obesity may increase collapsibility of the upper airway in males compared with females (45, 60).

Posture greatly influences upper airway mechanics. The supine posture challenges the upper airway, as the weight of the mobile tongue tends to close it. Indeed, some OSA patients experience more apneas and hypopneas when supine compared with the lateral position (12, 63), in whom preventing adoption of the supine position when asleep can be an effective treatment (12). Head position can also influence upper airway collapsibility. In children, neck rotation and the prone position increased upper airway collapsibility, but did not appear to affect passive stiffness (as measured by the pressure-area relationship) (32). Under anesthesia, head extension reduces airflow collapsibility, and flexion increases collapsibility (37, 87) and can change the site of collapse (87). Head rotation did
not affect collapsibility (87). These differences have been attributed to tracheal traction, although Isono and colleagues (37) suggest that the compliance of the airway walls decreased with neck extension due to increases in airway cross-sectional area. Jaw position may also influence passive collapsibility, with an open mouth increasing collapsibility, likely by narrowing the oropharynx (37). Pharyngeal collapsibility also increases with age (24), but this is paralleled by an increase in obesity and airway resistance, so this appears likely to be related to airway narrowing rather than specific age-related changes in tissue mechanics. However, an additional factor is the apparent deterioration of the reflex response of the genioglossus muscle with age (48).

Recently, the nocturnal rostral shift of fluid has been suggested to increase upper airway collapsibility (18, 95). This may reflect increased mucosal edema, which would narrow the airway and provide a soft surface layer on the pharyngeal wall (25). In heart failure, fluid accumulates in the neck of males more than in females (94), which may result in a higher fluid pressure (and/or tissue volume) in the pharyngeal wall and increase the risk of collapse. The magnitude of this effect and its contribution to OSA pathophysiology are not yet clear (for review, see Ref. 89).

DYNAMIC BEHAVIOR OF UPPER AIRWAY TISSUES

Dynamic behavior of the upper airway tissues results from central and reflex-derived muscle activity, as well as loads applied...
to the tissues, including respiratory-related changes in intraluminal pressure. The dynamic behavior encompasses muscle contraction, pharyngeal wall deformation, and possible changes in tissue stiffness due to muscle contraction (for which there is presently no data), all of which interact to affect airway caliber.

Neural drive to the upper airway muscles involves both tonic and phasic components (51, 52, 65, 69), but the mechanical effects of this drive are less clear. Imaging studies have shown that the airway caliber changes dynamically during respiration, both awake and asleep (8, 16, 70, 71), but there is considerable variability in changes in airway size and tissue motion. Recent studies using tagged MRI that track the movement of the soft tissues around the airway suggest that genioglossus typically moves anteriorly during inspiration (by 0.5–2 mm) in awake, healthy subjects, presumably to counteract the negative pressure in the airway, and relaxes posteriorly during expiration (8, 15, 16). Adding inspiratory resistance, which lowers the negative pressure in the airway required to maintain airflow, reduces this anterior motion [from a mean peak displacement of 0.48 ± 0.09 to 0.15 ± 0.09 mm (15)], reflecting a shift in the balance of forces between upper airway dilation and airway pressure. In OSA patients, different patterns of tissue motion occurred (Fig. 4 is a still of the animated video file found in Supplemental Fig. S1; the online version of this article contains supplemental data). Many severe patients exhibit little or no movement. Others had dilatory tissue motion in some regions, while other regions moved simultaneously to narrow the airway (8, 85). This has been termed “bidirectional” motion (8). Such complex motion indicates either poor coordination of neural drive to regions of the genioglossus, or the effect of a muscular hydrostat, whereby tissue contraction in one region expands an adjacent region. In subjects with a confined intramandibular volume, there may be no “spare space,” resulting in encroachment of noncontracting tissues on the airway lumen (Fig. 1C). Notably, the older, higher BMI subjects without OSA had larger, more uniform airway dilation during inspiration than the younger lean controls in the earlier studies, indicating that their airways were able to adapt dynamically to the challenge of maintaining airway patency while supine (8). The neuromechanical mechanisms underpinning these differences in motion patterns remain to be elucidated. During sleep, the activity of inspiratory phasic motor units in the genioglossus and tensor palatini decreases, while the tonic component is little changed (56, 91). This decrement in neural drive is larger in older persons (92). This would reduce the phasic dilation of the airway during sleep. However, this reduction of phasic activity occurs in both healthy subjects and OSA patients. In the context of the motion studies above, where the controls had larger phasic airway dilation awake and some OSA patients had little phasic dilation, this could mean that airway patency asleep might be more dependent on the passive stiffness of the airway [which is higher in control subjects (6)], or that, in healthy subjects, the remaining phasic activity is sufficient to keep the airway open. The contribution of this dynamic motion to the maintenance of airway patency during sleep is poorly understood. Currently, we do not understand the mechanical significance of changes in the balance between phasic and tonic activity of upper airway mus-

![Uniform dilation](Uniform dilation) ![Oropharyngeal dilation](Oropharyngeal dilation) ![Bidirectional motion](Bidirectional motion) ![Minimal motion](Minimal motion)

Fig. 4. Different patterns of tongue motion observed during quite awake breathing (see animated video file; adapted from Ref. 8). The uniform dilation pattern was typical of overweight and obese healthy control subjects. The oropharyngeal motion was typical of young lean subjects and mild OSA patients. The bidirectional motion pattern was most commonly observed in low-to-moderate severity OSA patients, and the minimal motion pattern was most common in moderately severe to severe OSA patients. However, considerable variability was observed, with some subjects exhibiting different motions patterns in different breaths within an imaging session.
cles (especially genioglossus) during wakefulness and sleep and the effect it may have in OSA.

In young, lean subjects, Cheng et al. (16) found that the lateral walls of the upper airway moved minimally during the respiratory cycle, but with added inspiratory resistance, the lateral walls moved medially during inspiration (15). Thus the additional load on the tissue was not counterbalanced by the tissue passive tension and muscle activity. In mild-to-moderate OSA patients and older, heavier control subjects, the lateral walls moved inward during inspiration, but the more severe patients had little lateral wall movement (8). Lateral wall movement decreased with increasing apnea hypopnea index. These studies also suggest that there is more breath-to-breath variation in tissue movement in OSA patients than in healthy subjects (8) and could indicate that the upper airway in OSA is close to a critical balance point, where small variations in the local airway pressure result in greater variation in airway wall motion and thus airway caliber. This remains to be determined. Studies of dynamic airway cross-sectional area show that the airway enlarges during inspiration in healthy subjects, but there is little widening in OSA patients (70–72). Using optical coherence tomography, Walsh and colleagues (86) found no consistent pattern of airway dimensional changes during the respiratory cycle in awake supine OSA patients and control subjects. The largest airway caliber occurred during inspiration in some subjects and expiration in others. This may reflect the complexity and individual variation in genioglossus and lateral wall motion documented using other techniques (e.g., Refs. 8, 15, 16). Imaging studies conducted asleep are limited, mostly focus on static images (e.g., Ref. 82), and have often used drugs that may influence muscle activity and local pharyngeal sensation to maintain sleep (e.g., Ref. 54). This complicates interpretation of the results. Development of acoustically quiet MRI is a promising advance (77).

Other Factors Influencing Airway Dynamics

In addition to the factors already mentioned, surface tension resists the separation of adjacent surfaces and resists upper airway opening (44). Reduction of surface tension using surfactants reduces the pressure required to passively reopen the airway, and both the PCr in the airway and also apneas and hypopneas (43, 44). One study showed that surfactant might also reduce airway resistance by reducing fluid bridging between nearby pharyngeal surfaces (55).

The effects of anatomical and postural variations on upper airway dynamics, beyond the passive changes noted above, are not yet known, but there are hints that there are effects. Odeh and colleagues (57) noted that changes in head position in the dog altered the mechanical effectiveness of the dilator muscles, particularly genioglossus, and suggested this may be due to changes in muscle length (59). However, it is not known whether this occurs in humans, nor if the changes in muscle length in humans are similar to those in dogs, given the substantial differences in anatomy. Respiratory muscles acting on the chest wall are recruited in an orderly way, according to a gradient of decreasing mechanical advantage (10, 20), but the action of this principle of neuromechanical matching is not established for the upper airway. The precise regional activation across and within the upper airway muscles, such as genioglossus, is unknown. This information may be important because different regions of the muscle have different mechanical effectiveness in dilation of the airway, and anatomical variations that are common in OSA could alter mechanical effectiveness. For example, a lower hyoid may reduce the mechanical advantage of the genioglossus muscle fascicles.

Clinical Implications

Most currently accepted OSA treatments manipulate the mechanics of the upper airway. The “gold standard” treatment, CPAP, has its primary effect by “pneumatically splinting” the airway open (79) (Fig. 5A). This positive pressure also reduces muscle activity (78), but the pressure from CPAP offsets any reduction in dilatory forces. CPAP may also reduce fluid accumulation in the neck (94). Such accumulation would favor airway closure by increasing tissue mass and/or tissue pressures (18, 25, 95).

Mandibular advancement splints, by bringing the mandible forward, enlarge the oral cavity (14, 36) (Fig. 5B). They are only fully effective for about one-half of OSA patients (3) and seem to work better for women, those with smaller neck circumference, with predominantly oropharyngeal collapse, and mild to moderate severity patients (13). Predicting who will benefit is an unsolved clinical challenge. Using tagged MRI, Brown and colleagues (9) recently observed three patterns of tissue deformation during mandibular advancement: 1) the whole tongue moved forward “en bloc” (common in OSA patients of mild-moderate severity); 2) only the inferior portion of the tongue moved forward; or 3) the posterior tongue did not move, but the whole tongue elongated (common in severe OSA patients). The results were not compared with splint efficacy, so it is unclear whether these different patterns might reflect mechanisms of splint action. A direct soft tissue connection from the ramus of the mandible to the lateral pharyngeal walls was also noted, which may account for the observed enlargement of the airway laterally. The magnitude of this lateral wall motion varied considerably. Viscoelasticity of the soft tissues may also play a role, as the tissue will slowly relax after mandibular advancement and “creep” backwards due to the effects of gravity when in a supine position and negative airway pressure during inspiration, but this has not been studied. Although splints have been proposed to increase average dilator muscle activity (38, 93), their effect on dynamic airway motion is not yet known.

Other available oral appliances typically manipulate the tongue directly, either by stabilizing its position, or drawing it forward, thus preventing it from collapsing back to obstruct the airway (11, 14, 21).

Hypoglossal nerve stimulation is a novel treatment that stimulates the dilator muscles during inspiration, thus actively dilating the airway and preventing collapse (Fig. 5C). It is discussed in detail in another minireview in this series (73a).

An important question is how tissue mechanical behavior (movement and stiffness) is related to neural drive to the upper airway musculature, as assessed by electromyography (EMG). While the level of EMG during quiet breathing has long been assumed to be tightly linked to upper airway function, recent evidence questions this link. Two detailed studies of the behavior of single motor units in genioglossus indicate that neural drive during quiet breathing (awake) in severe OSA patients retains the typical tonic and phasic patterns of activity with only small changes in firing rates and inspiratory timing.
compared with the behavior of units in healthy subjects (67, 68). These are likely to signify neuropathic changes in the genioglossus in OSA (66). Recent studies of tongue motion and stiffness in severe OSA patients indicate that neural drive to genioglossus does not dilate or stiffen the airway (6–9). Furthermore, Dotan and colleagues (23) recently demonstrated that the relationship between genioglossus EMG and its mechanical action during propofol anesthesia was tenuous. Muscle contractility was preserved, but there was no flow change, despite large increases in dilator muscle EMG during flow limitation. Thus the background “physiological” level of drive was insufficient to either dilate the airway, or restore the tongue’s passive stiffness to “normal.” The mechanisms underpinning this dissociation between mechanics and neural drive require further study.

CONCLUSIONS

This assessment of the mechanical factors involved in patency of the upper airway demonstrates the complexity of this dynamic neuromechanical system. While some factors have been studied, many have not, and the interactions between biomechanics of the tissues, neural control of the muscles, and airflow have yet to be fully understood. In young, normal-weight, healthy humans, the upper airway is “dynamically stable” and responds so as to maintain patency throughout the respiratory cycle. Obesity increases demands on the upper airway as a dynamic system, but, in healthy subjects, patency is maintained. However, in OSA patients, the upper airway is “critically stable,” such that small changes in conditions (e.g., posture, pressure, sleep state) cause instability and upper airway narrowing or collapse. In OSA, it seems that there is a dissociation between increases in neural drive to the upper airway muscles and evoked contractile force. Certainly, the neural drive in OSA is insufficient to compensate for unfavorable passive upper airway mechanics, arising from a narrow airway and more compliant wall tissues. Evolutionary changes in the upper airway to facilitate speech have delivered a structure that is not only complex in terms of neural control and tissue mechanics, but one that is poorly adapted to the vicissitudes of obesity and aging.

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Author contributions: L.E.B. and S.C.G. conception and design of research; L.E.B. prepared figures; L.E.B. and S.C.G. drafted manuscript; L.E.B. and S.C.G. edited and revised manuscript; L.E.B. and S.C.G. approved final version of manuscript.

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