Sleep-related breathing disorders · 2

Pathophysiology of obstructive sleep apnoea

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Obstructive sleep apnoea is a disorder characterised by recurrent sleep-induced collapse of the pharyngeal airway.[1] The principal sequel, hypersomnolence (or sleepiness during the day), results from the repeated arousals required to reopen the airway and resume breathing and thus poor sleep quality during the night in these patients.[2] The recurrent hypoxaemia and hypercapnia which characterise sleep apnoea may also lead to both pulmonary[3] and systemic hypertension,[4] cardiac arrhythmias,[5] and possibly decreased survival.[6] As a result, this disorder can impact on the health and wellbeing of the afflicted individual. This review will address the pathophysiology of this disorder with the principal focus being the mechanisms that lead to pharyngeal collapse during sleep. No attempt will be made to address exhaustively every possible hypothesis regarding this sleep-induced airway event. However, prominent theories will be discussed. In addition, a somewhat briefer discussion on the mechanisms of apnoea termination will be included.

Pharyngeal collapse

The principal problem in the patient with obstructive apnoea is the collapse of the pharyngeal airway (fig 1) which characteristically occurs at the onset of sleep in these individuals.[1] Although respiratory effort generally continues, the obstructed (or largely obstructed) pharyngeal airway prevents effective ventilation producing either apnoea (total respiratory cessation) or hypopnoea (a substantial reduction in ventilation). In either case, hypoxia and hypercapnia quickly develop necessitating arousal to re-establish airway patency and normal ventilation.[7] The location of this obstruction is virtually always between the choanae and the epiglottis, generally either behind the uvula and soft palate (the velopharynx), or behind the tongue (the oropharynx), or some combination of the two.[8] Rare reports of collapse of the airway at the level of the epiglottis have emerged,[9] but this is probably unusual.

PHARYNGEAL ANATOMY

To understand the sleep-induced collapse of the airway which characterises sleep apnoea, some knowledge of the anatomy and physiology of this region of the airway is required. The vulnerable segment between the choanae and epiglottis (fig 1) in man lacks substantial bony or rigid support. This is particularly true of the anterior and lateral pharyngeal walls. Thus, the patency of this segment of the airway is largely dependent on the activity of various pharyngeal dilator muscles.[10] As long as these muscles are sufficiently active, patency of the airway is maintained. However, loss of muscle activity in some or all of these muscles could diminish the size of the airway or lead to complete collapse. Thus, an important relationship exists in man between the anatomy of the pharyngeal airway and the dilator muscles controlling the size of the airway lumen, a relationship that is likely to vary between subjects. An individual with an anatomically large pharyngeal airway may be minimally dependent on dilator muscle activity with decrements in such activity leading to only small increments in pharyngeal airway resistance.[11] On the other hand, an individual with an anatomically small airway may require substantial pharyngeal dilator muscle activity
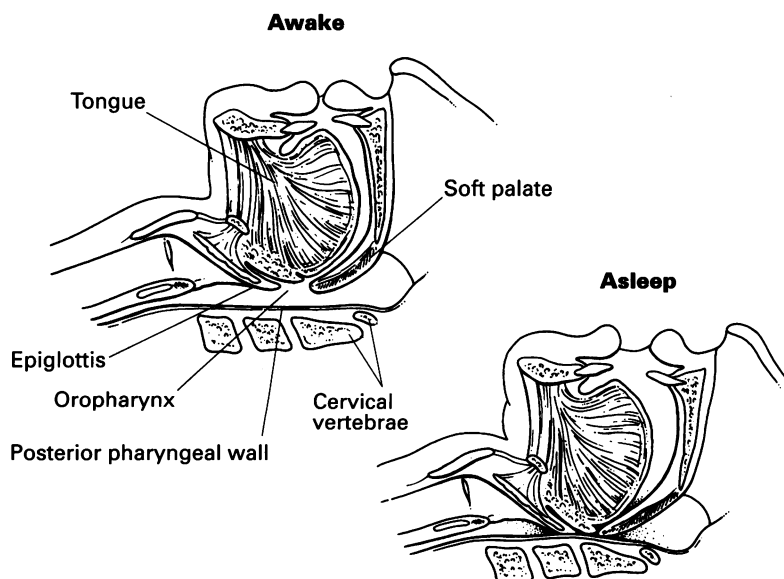

Figure 1 *Diagrammatic representation of the pharyngeal airway of a patient with apnoea. During wakefulness airway patency can be maintained. During sleep collapse occurs as shown between the choanae and the epiglottis. Printed with permission from White.[52]*

to maintain patency.[12] In this individual a small decrement in muscle function may lead to large increases in airways resistance or complete collapse of the airway. Thus, the anatomy of the individual pharyngeal airway is likely to be important.

Why one individual has an anatomically large pharyngeal airway and another individual a small one is poorly understood. However, airway size is affected by a number of variables. Firstly, obesity influences the anatomy of the upper airway as weight gain commonly leads to increasing airways resistance. Whether this is a product of direct fat deposition around the pharyngeal airway or relates to less obvious events remains unexplained. However, the relation between obesity and size of the airway seems clear.[13 14] Secondly, aging may influence the anatomy of the airway with older individuals tending to have anatomically smaller and possibly more collapsible airways.[13 14] Finally, genetically-driven individual variability in jaw position, tonsillar tissue, tongue size, etc may all influence the size of the pharyngeal airway. Thus, several variables combine to determine the size of the airway in an individual.

PHARYNGEAL MUSCLE FUNCTION
The muscles responsible for the maintenance of patency of the upper airway are numerous and are, at best, incompletely understood.[10] Those believed to be most important fall into three groups: (a) the muscles influencing hyoid bone position (geniohyoid, sternohyoid, etc), (b) the muscle of the tongue (genioglossus), and (c) the palatal muscles (tensor palatini, levator palatini, etc). These muscles behave in a variety of ways. Most contract vigorously on inspiration (much like the diaphragm), presumably stiffening and dilating the upper airway.[15 16] They are therefore called inspiratory phasic muscles and are exemplified by the genioglossus muscle, the principal muscle of the tongue (figs 1 and 2). These muscles counteract the normal collapsing influence of neg-

ative pressure in the airway which is present during inspiration. Thus, airway patency during inspiration is the product of the inherent anatomy (discussed above), plus the combined influences of negative pressure which would tend to collapse the airway and pharyngeal muscle activity which attempts to dilate it.[1] During expiration these inspiratory phasic muscles have substantially reduced activity as intraluminal airway pressure is positive and there is little tendency for the airway to collapse. However, some level of expiratory activity is virtually always present and is called tonic activity. It would seem reasonable to assume that the activity of these inspiratory phasic upper airway muscles is strongly influenced by central neurons that have an inspiratory phasic pattern of activation (fig 3). These are called central respiratory neurons and have been identified in several areas in the brain stem. They control the activity of muscles such as the diaphragm and will influence these upper airway muscles as well.

Other muscles such as the tensor palatini have little or no inspiratory phasic activation,[17] but demonstrate a more constant level of activity throughout the respiratory cycle. Such muscles are called tonic or postural muscles. Despite this absence of clear respiratory cycle-related activity, these muscles are important in the maintenance of airway patency during both inspiration and expiration. As there is no clear inspiratory phasic activation pattern, one must assume that the activity of these muscles is not directly controlled by central respiratory neurons. Their activity is more likely to be controlled by tonic or postural neurons with a more constant firing pattern unrelated to the respiratory cycle (fig 3).

The activity of both types of pharyngeal dilator muscles (inspiratory phasic and tonic) is influenced by several stimuli. Firstly, standard respiratory chemical stimuli (rising PCO_2 and falling PO_2) can substantially augment the activity of these muscles.[18 19] More importantly, however, negative pressure (which would tend to collapse this segment of the airway) can markedly activate these muscles, preventing collapse. This has been observed in animals for
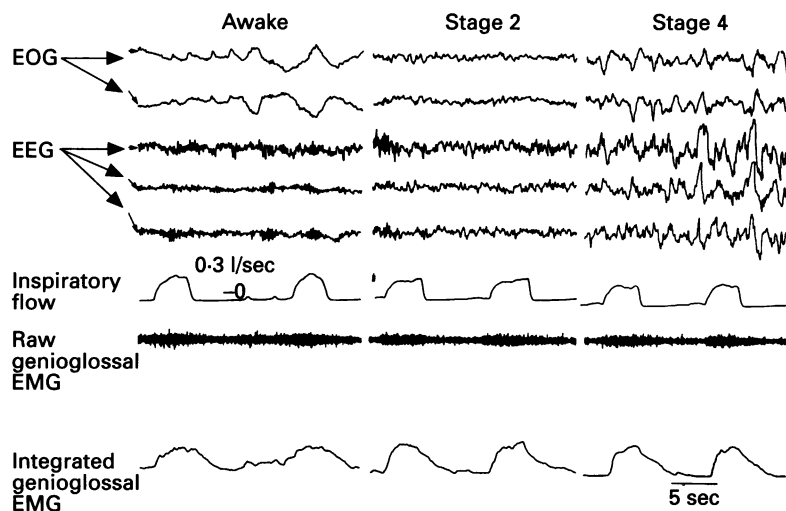
Figure 2   Sample recording from a subject illustrating phasic rise in airways resistance (Raw) and integrated genioglossal EMG activity during inspiration (corresponding to positive deflection in inspiratory flow signal) during wakefulness and stages 2 and 4 of non-REM sleep. EOG = electro-oculographic channel; EEG = electroencephalographic signals.
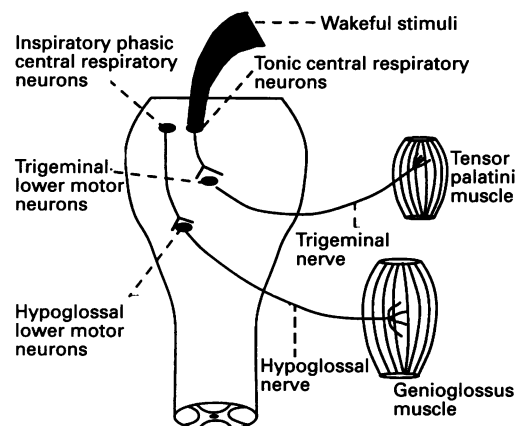
Figure 3   Scheme showing the influence of inspiratory phasic versus tonic central respiratory neurons on the activity of the dilator muscles of the upper airway. The tonic central neurons, unlike the phasic ones, are dependent on wakeful stimuli to maintain activity.
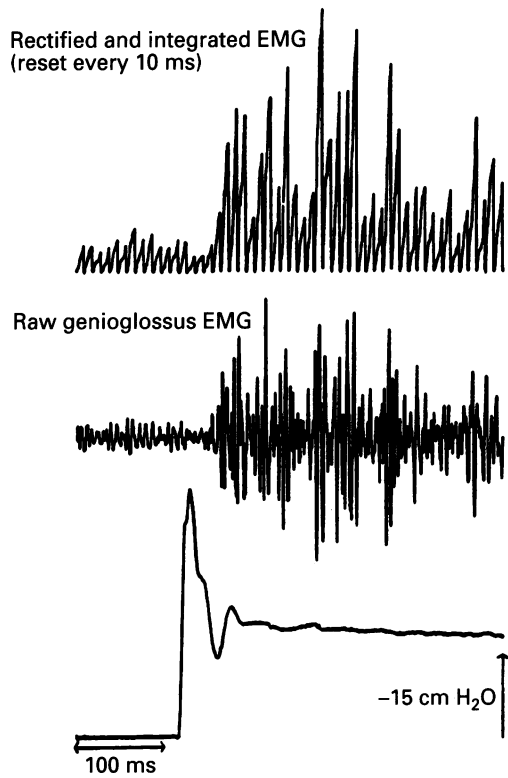
Figure 4   Single response in one subject showing
activation of the genioglossus muscle following a 15 cm
H_2O negative pressure change with the glottis closed. Note
the rapidity of the pressure change (0–90% time = 4 ms)
and the short latency of activation from the onset of the
pressure change (45 ms). Raw = airways resistance.
Printed with permission from Horner et al.[22]

years[20][21] and has recently also been shown in
humans.[22][23] A pulse of negative pressure in the
pharyngeal airway of a normal man will lead
to considerable augmentation in the activity
of these pharyngeal dilator muscles, thereby
preventing collapse of the airway (fig 4). This
negative pressure reflex response seems to be
driven by pressure-sensitive airway receptors
(fig 5) as pharyngeal anaesthesia diminishes or
abolishes the reflex.[24] The activity of these
muscles, at least during wakefulness, is thus
precisely controlled both to maintain upper
airway patency and to allow hyperventilation
should hypoxia or hypercapnia develop.

From the above discussion a clear concept
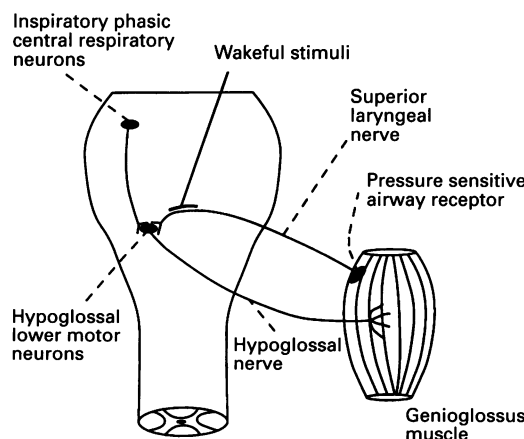should emerge. Whether an individual develops

Figure 5   Schematic representation of several mechanisms
which control genioglossal muscle activity.

upper airway collapse and apnoea during sleep
will depend on two variables: (a) the influence
of sleep on the activity of the various pharyngeal
dilator muscles, and (b) how dependent that
individual's airway is on the activity of these
muscles. If pharyngeal dilator muscle activity
was completely maintained during sleep in
everyone, it seems unlikely that obstructive
apnoea would be a clinical problem. Along
these same lines, if the pharyngeal airway was
rigidly supported by bone or cartilage, collapse
of the airway would be a virtual impossibility
and apnoea would not occur. However, neither
of the above is true and the relation between
the anatomy and muscle function in the upper
airway becomes critical during sleep.

SLEEP AND THE PHARYNGEAL MUSCULATURE
Normal subjects

Sleep is not a uniform state and is composed
of several stages. However, in practical terms
it can be divided into rapid eye movement
(REM) and non-rapid eye movment (non-
REM) sleep. During REM sleep dreaming
clearly occurs which probably does not occur
during non-REM sleep. These two types or
stages of sleep are also quite different in various
other physiological ways. Thus, it is difficult to
make broad statements about sleep as a whole.
These physiological differences between REM
and non-REM sleep also apply to the mech-
anisms controlling the pharyngeal muscles. Al-
though only non-REM sleep is considered in
this review, the principles discussed also apply
to REM sleep although the underlying neural
mechanisms may be different.

It seems clear that sleep, even in normal
subjects, affects the activity of the pharyngeal
dilator muscles although not in a uniform man-
ner. Some muscles seem to lose activity during
sleep whilst in others it is reasonably well main-
tained.[16] This differential effect of sleep on
muscle activity seems to relate to the phasic
nature or activation pattern of the muscle.
Muscles with a prominent inspiratory phasic
pattern of activation (such as the genioglossus
or geniohyoid muscle) largely maintain their
activity during non-REM sleep,[15][16] particularly
the phasic component of this activity (fig 2).
However, tonic activity may fall somewhat in
these muscles.[15] Tonic muscles or muscles with
little inspiratory phasic pattern seem to lose
activity during sleep as exemplified by the ten-
sor palatini.[17] With sleep onset the electro-
myogram (EMG) of the tensor palatini muscle
begins to fall and continues to drop pro-
gressively through the various stages of non-
REM sleep (fig 6). By stage 4 sleep the tensor
palatini is only about 20–30% as active as
during wakefulness. This differential effect of
sleep on the activity of tonic versus phasic
muscles probably relates to the quite different
effects of sleep on the central respiratory neur-
ons controlling their activity (fig 3) as shown
by Orem and coworkers.[25][26] In chronically in-
strumented cats, Orem demonstrated a reas-
onable maintenance of the activity or frequency
of firing of brainstem neurons during non-
REM sleep with an activity pattern closely

EOG

EEG

Tensor palatini Raw EMG

Tensor palatini MTA EMG
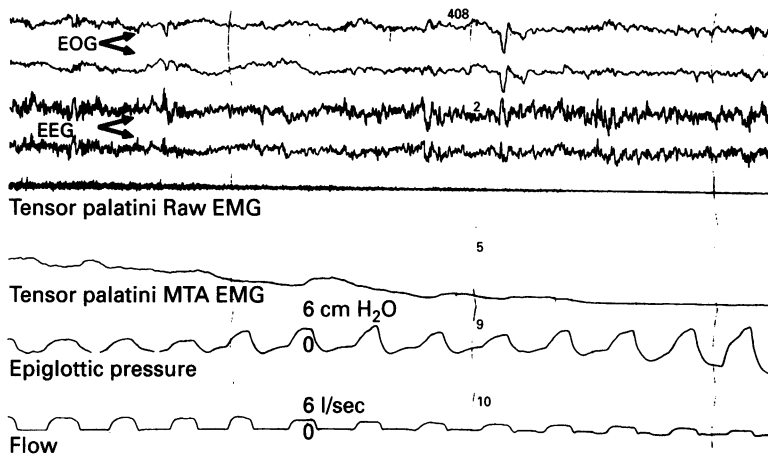
6 cm H₂O

Epiglottic pressure

6 l/sec

Flow

Figure 6   Representative airways resistance (Raw) data during transition from wakefulness to sleep. A fall in tensor palatini moving time average (MTA) electromyogram (EMG) and associated rise in oesophageal pressure with falling inspiratory flow are shown indicating increased airway resistance. EOG = electro-oculogram; EEG = electroencephalogram. Printed with permission from Tangel et al.[17]
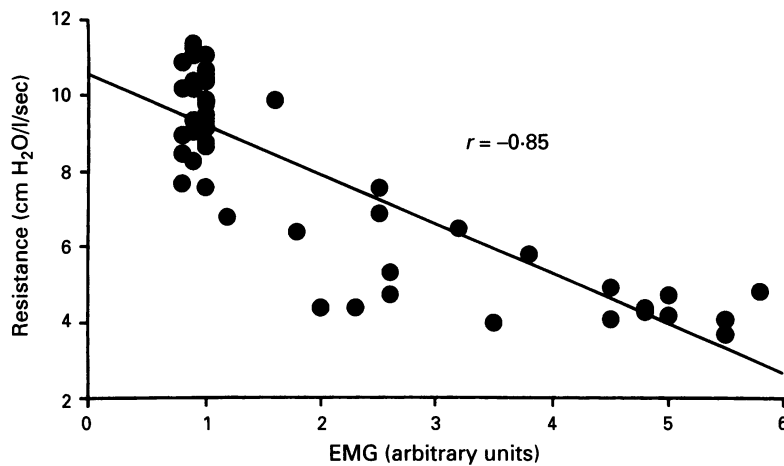
$r = -0.85$

Figure 7   Linear regression analysis demonstrating inverse relation between tensor palatini moving time average EMG and upper airway resistance. Each point represents a 30s average for each variable in one subject across wakefulness and all stages of sleep. Printed with permission from Tangel et al.[17]

related to the respiratory cycle (inspiratory neurons).[26] These neurons therefore seemed to be minimally dependent on the waking state or wakeful stimuli to maintain activity. On the other hand, neurons whose firing pattern had little relation with the respiratory cycle showed substantial decrements in activity during sleep.[26] These neurons are highly dependent on wakefulness or wakeful stimuli to maintain function. To the extent that neurons firing predominantly during inspiration influence the activity of inspiratory phasic muscles and tonic neurons influence tonic muscles (fig 3), Orem's studies may explain the differential effect of sleep on the activity of the various pharyngeal muscles.

Despite this maintenance of activity in many pharyngeal dilator muscles during non-REM sleep, upper airway resistance rises significantly during the night in virtually everyone.[27 28] This sleep-induced increment in airway resistance must therefore be attributed to the decrement in tonic muscle activity described above. Such a relationship has been demonstrated. Tangel et al[17] observed a clear correlation between falling tensor palatini EMG and upper airway resistance in a group of normal men (fig 7).

One would have to conclude, therefore, that sleep-induced decrements in the firing frequency of non-phasic central respiratory neurons leads to decrements in the activity of important pharyngeal dilator muscles (such as the tensor palatini) which, in turn, leads to decreased patency of the airway or rising airway resistance even in otherwise completely normal individuals as they sleep.

Patients with obstructive apnoea

To understand how sleep influences pharyngeal muscle function in patients with obstructive sleep apnoea one must first understand the pharyngeal anatomy of the patient with apnoea and how this anatomy influences waking muscle function.

It seems clear from several studies using a number of different imaging techniques that the lumen of the pharyngeal airway of patients with obstructive apnoea, even during wakefulness, is anatomically small. Investigators have used computed tomographic scanning,[29] acoustic reflection,[30] and the measurement of airway resistance,[31] all with the same result; the patient with obstructive apnoea has a structurally small airway. Why the airway is small may vary from one patient to the next. In some cases this may be due to fat deposition in the neck and thus the problem is associated with obesity. In others the mandible may be small (micrognathia) yielding reduced upper airway size. In still others tonsillar hypertrophy may render the airway small. Thus, a common variable in virtually all patients with obstructive apnoea is a structurally small pharyngeal air space.

As stated previously, the activity of the pharyngeal dilator muscles is, during wakefulness, tightly controlled in an attempt to maintain airway patency. This activity is primarily driven by negative pressure reflex responses of the airway,[22 23] although other neural mechanisms may also be active (fig 5). In the apnoea patient with an anatomically small airway (as described above) these reflexes are activated during wakefulness leading to augmented dilator muscle activity in an attempt to overcome the anatomical limitation.[12] This phenomenon has been shown in the genioglossus muscle (fig 8).
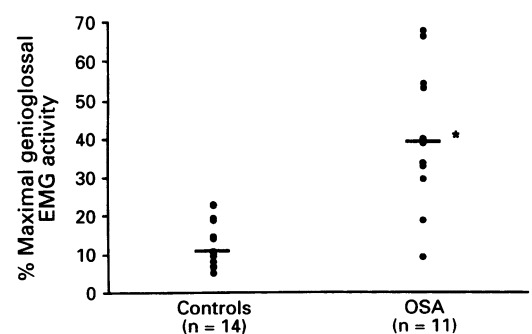
*Figure 8   Peak phasic genioglossal EMG activity. Cumulative data from all subjects and patients which show that, in the basal state, the genioglossal muscle functions at a higher percentage of maximum in patients with obstructive sleep apnoea (OSA) than in controls. *p<0·05 versus controls. Printed with permission from Mezzanotte et al.*[12]
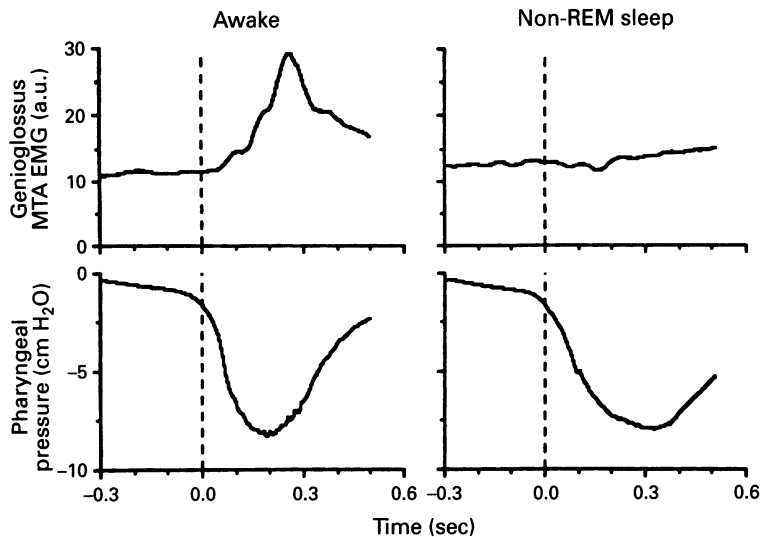
Figure 9 *Single average genioglossus response. Representative computer signal averaging of genioglossus moving time average (MTA) electromyogram (EMG) and pharyngeal pressure in one subject showing mean data from 75 negative pressure generations (NPG) both when awake and during non-rapid eye movement (non-REM) sleep. Vertical dashed lines denote onset of the NPG. Note the large genioglossus EMG response to NPG (with EMG latency of 30 ms) during wakefulness which is markedly reduced during sleep despite similar negative pressure. Printed with permission from Wheatley et al.[23]*

In patients with apnoea with a small airway this muscle functions at nearly 40% of its maximal capacity during wakefulness while the genioglossus muscle in normal subjects functions at only about 12% of maximum.[12] Thus, clear differences in muscle activity exist in these groups. Similar observations have also been made in an animal model of sleep apnoea.[32] Again, we believe this increased muscle activity represents a neuromuscular compensation for an anatomically small airway. That negative pressure drives this augmented muscle activity is suggested by the observation that positive pressure (CPAP) reduces genioglossal muscle activity in patients with apnoea to nearly normal levels.[12] One would have to assume therefore that, without this stimulated muscle
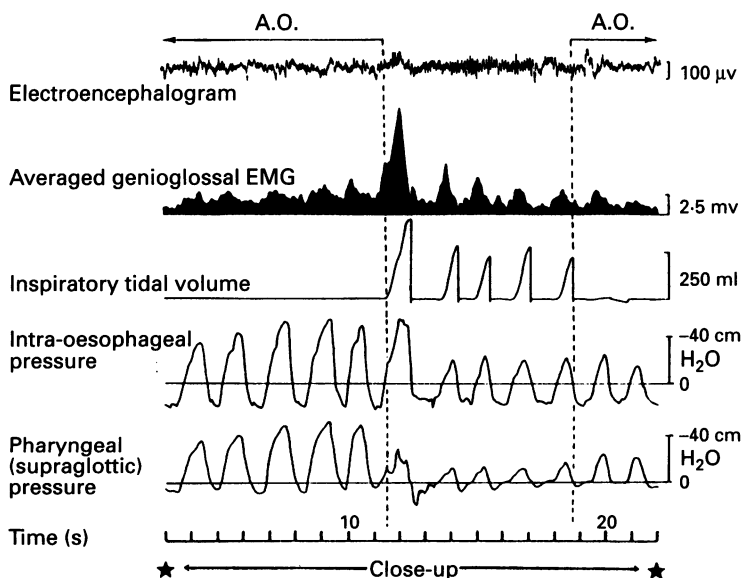

Figure 10 *Sleep records from a patient with apnoea showing evidence of arousal (alpha EEG activity) just prior to termination of the obstructive apnoea and loss of this alpha EEG with onset of airways obstruction. Note loss of genioglossal EMG at sleep onset which is quite different from that observed in normal subjects (fig 2). Printed with permission from Remmers et al.[1]*

activity, the airway of the patient with apnoea would collapse or have a very high resistance even during wakefulness.

Sleep is a state that is associated with the loss of, or a significant reduction in, various neural reflex mechanisms. This is certainly the case for postural, spindle-driven reflexes[33-35] and appears also to be true for the negative pressure reflexes in the upper airway.[23] As stated above, a pulse of negative pressure in the pharynx of normal humans leads to a substantial increase in genioglossal muscle activity. With the onset of non-REM sleep this negative pressure response in normal volunteers is markedly reduced[23] or lost completely (fig 9). To the extent that the augmented muscle activity present during wakefulness in the patient with apnoea is driven by this reflex, it should also be lost during sleep leading to a decrement in muscle activity to normal or near normal levels. Again, this seems to be the case. Studies of genioglossal muscle activity in patients with apnoea[136] indicate a substantial reduction in muscle activity at sleep onset (fig 10) which is quite different from that which is observed in normal subjects as described above.[1617] The genioglossus muscle has an inspiration phasic activation pattern and thus its activity is relatively well maintained during non-REM sleep in normal individuals (figs 2 and 3). In the patient with apnoea genioglossal muscle activity falls at sleep onset,[135] which we interpret not as a normal effect of sleep on the muscle but as a loss of the neuromuscular compensation present during wakefulness. With this decrement in muscle activity in the apnoea patient patency of the airway becomes compromised and the apnoea or hypopnoea begins.

One would have to assume that sleep has a similar effect on the activity of tonic postural muscles (such as the tensor palatini) in the patient with apnoea as has been shown in normal subjects. Thus, this activity should fall in both groups. The sleep-induced decrement in muscle activity in the patient with obstructive apnoea is therefore likely to be a product of both: (a) the loss of neuromuscular compensation in all muscles in which this phenomenon is present, and (b) the normal decrement in the activity of tonic postural muscles. This combined effect of sleep leads to muscle activity that is inadequate to maintain the patency of the airway.

OTHER THEORIES OF PHARYNGEAL COLLAPSE IN OBSTRUCTIVE SLEEP APNOEA

It should be stated that there is not complete uniformity of opinion regarding the mechanism of airway collapse in patients with obstructive sleep apnoea. Although most investigators would agree that patients with apnoea generally have an anatomically small pharyngeal airway and that airway collapse is associated with a sleep-induced decrement in pharyngeal dilator muscle activity, the explanation for changing levels of muscle function during sleep is controversial. Some would argue that the waxing and waning of muscle activity that characterises sleep apnoea is more a product of instability of
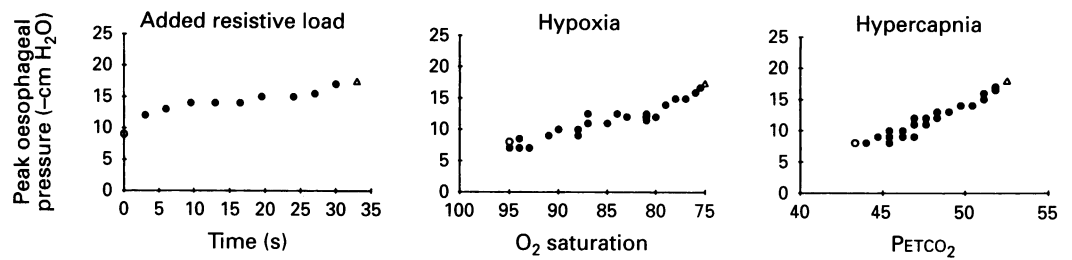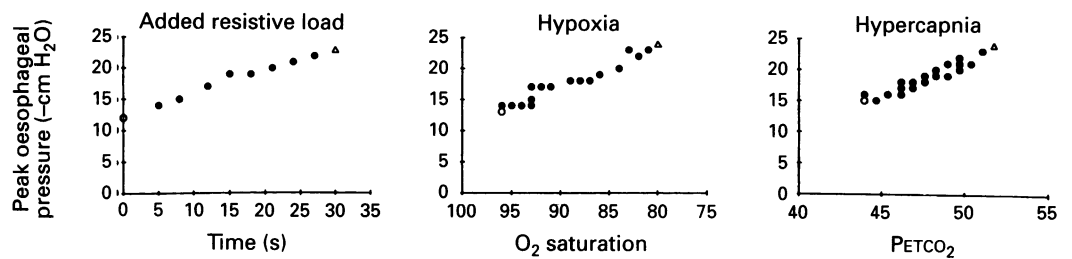
Subject 4

Subject 6

Figure 11 Plots of peak negative inspiratory oesophageal pressure for three different respiratory stimuli at baseline (○), during stimulated ventilation (●), and for the breath preceding arousal from sleep (△) for two different subjects. Peak negative oesophageal pressure begins at similar baseline levels and progressively increases until arousal results at a level that is similar within, but different between, the two subjects. Printed with permission from Gleeson et al.[48]

intrinsic ventilatory control than purely the effect of sleep on muscle activity in an individual with a small airway.[36] These investigators would argue that this instability in the basic mechanisms that normally control ventilation leads to a waxing and waning of muscle activity and that apnoea occurs when pharyngeal dilator muscle activity is low and diaphragmatic activity relatively high. Thus, pharyngeal muscle function does not adequately compensate for the negative pressure in the airway (driven by the diaphragm) and the upper airway collapses.

Others would suggest that sleep-induced collapse of the airways may be more a product of poor coordination of diaphragmatic versus upper airway muscle activity during sleep than a real loss of upper airway muscle function.[37] These studies suggest that delayed activation of upper airway muscles in the patient with apnoea may lead to substantial negative pressure when the pharyngeal muscles (compared with the diaphragm) are relatively inactive and thus the airway is collapsible. Whether this represents a primary defect in muscle control in the patient with apnoea or a secondary phenomenon resulting from the apnoea itself is unclear at this time.[37]

Finally, there is some evidence that changing muscle activity alone is not responsible for the development of obstructive sleep apnoea. These investigators argue that factors such as mucosal adhesiveness[38] or vascular perfusion of the pharyngeal airway may influence airway patency or collapsibility, or that loss of tracheal traction[39] on the upper airway (from decreased lung volume during sleep) substantially reduces the stiffness or rigidity of the pharynx. All of these hypotheses are likely to have some validity

in explaining the complex relation between sleep, anatomy of the airway, and pharyngeal muscle function.

Termination of apnoea

Once the patient falls asleep and the apnoea or hypopnoea begins, ventilation by definition becomes inadequate to meet the metabolic demands of the body resulting in hypoxaemia and hypercapnia. How rapidly hypoxaemia develops probably depends on a number of variables[40] including: (a) the Po_2 or arterial oxygen saturation level when the apnoea began, (b) the oxygen stores in the body which relate primarily to the lung volume at the point of apnoea, and (c) to a lesser extent whether ventilatory effort is occurring against the obstructed upper airway. The ultimate severity of the hypoxaemia depends, however, not only on the speed with which Po_2 falls but also on the duration of the apnoea. A long apnoea will generally lead to more severe hypoxaemia and assumedly hypercapnia than a shorter one. Thus, terminating the apnoea is important if severe hypoxaemia and hypercapnia are to be avoided.

Most current data would support the concept that termination of apnoea requires a transient arousal from sleep.[7] Sometimes this is quite obvious on the sleep record and at other times more subtle. However, most apnoeas require a brief arousal (whether cortical or subcortical) to activate the upper airway muscles and to reestablish airway patency and ventilation. Without such an arousal, profound hypoxaemia or even death might occur. Thus, arousal is the ultimate respiratory response to apnoea.

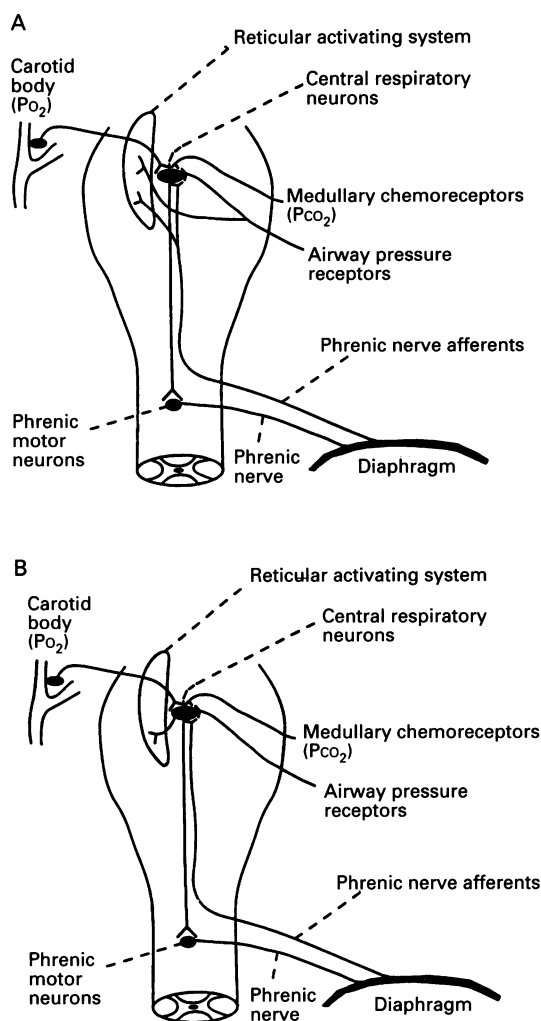To understand the mechanisms leading to

Figure 12 Scheme depicting two potential mechanisms by which increasing ventilatory effort could lead to arousal from sleep. (A) Hypoxia and hypercapnia stimulate increasing ventilatory effort which activates either phrenic (or other respiratory muscle) nerve afferent or airway pressure receptors which directly stimulate the reticular activating system causing arousal. (B) Increased central respiratory neuronal activity induced by the hypoxia and hypercapnia of apnoea impacts directly on the reticular activating system leading to arousal from sleep.

the arousal one must examine the events preceding it. As stated above, during an apnoea the individual becomes progressively more hypoxaemic and hypercapnic. Each is a clear ventilatory stimulant during wakefulness and, when combined, produces an even greater augmentation of ventilatory effort. These stimuli seem to have a similar effect on respiratory effort during sleep.[41-43] The sensitivity of this response (ventilatory effort versus rising P_{CO_2} or falling P_{O_2}) may be reduced during non-REM sleep and somewhat further reduced during REM sleep, but are clearly present and substantial during all stages of sleep.[41-43] Therefore, ventilatory effort increases progressively as the apnoea proceeds in the patient with sleep apnoea.[35] Thus, over the course of the apnoea a number of respiratory events occurs: (a) the P_{O_2} falls, (b) the P_{CO_2} rises, (c) ventilatory effort increases (greater respiratory muscle work), and (d) intra-airway pressure becomes progressively more negative. Any or all of these respiratory phenomena could be responsible

for the arousal which terminates the apnoea, with some research support for each. It has been postulated that (a) the arousal is mediated by pressure-sensitive receptors in the upper airway,[44] (b) that augmented carotid body output resulting from hypoxaemia awakens the individual,[45 46] and (c) that receptors sensitive to P_{CO_2} mediate arousal.[47] Each could potentially lead to increasing afferent neural traffic to the reticular activating system and arouse the individual; data are available to support each hypothesis.

A more unifying theory regarding this arousal mechanism has emerged in the last few years and substantial data suggest that it may be correct. Gleeson *et al*[48] proposed that respiratory-related arousal from sleep may relate more directly to increasing ventilatory effort itself than to any of the specific stimuli (hypoxia, hypercapnia, etc) causing the augmented effort. He observed that normal subjects were aroused from non-REM sleep (fig 11) at a relatively constant level of respiratory effort (peak oesophageal pressure) regardless of the respiratory stimulus used (hypoxia, hypercapnia, inspiratory resistive loading). This concept has, in general, been confirmed by a number of studies where either the effort produced by respiratory stimulation has been manipulated[49 50] or various combinations of chemical (P_{O_2}, P_{CO_2}) and mechanical (loading) stimuli were combined.[51] All seem to support the general concept that, within a given individual, respiratory arousal from sleep occurs at a relatively fixed respiratory effort regardless of what is stimulating ventilation.

How increasing ventilatory effort leads to arousal has not been directly studied. However, one could speculate that this arousal is a result of one of two mechanisms. Firstly, increasing afferent neural input from respiratory muscles or pressure-sensitive airway receptors could directly stimulate the reticular activating system thereby arousing the individual (fig 12A). Alternatively, the augmented output from the central respiratory neurons that mediate the increasing ventilatory effort during apnoea could synapse directly with the reticular activating system yielding arousal when their firing frequency or output is sufficiently high (fig 12B). Therefore, once central respiratory neuronal output (which is driven by the developing hypoxia, hypercapnia, etc) reaches a threshold level, arousal will occur because of direct connections between these respiratory neurons and the reticular activating system. Either hypothesis could be correct with considerable further investigation being required to sort this out. However, the link between increasing ventilatory effort and arousal from sleep seems clear.

Conclusions

From what has been said one would have to conclude that the primary defect in obstructive sleep apnoea is an anatomically small pharyngeal airway. During wakefulness the individual can compensate for this anatomical deficiency with augmented pharyngeal dilator

muscle activity thereby maintaining airway patency. With the onset of sleep the reflexes which drive this muscular compensation are diminished or lost leading to falling muscle activity and ultimately pharyngeal collapse. Thus, the apnoea begins. As ventilation is absent or substantially diminished Pco_2 will rise and Po_2 will fall. Both are clear ventilatory stimulants even during sleep and lead to progressively augmented respiratory effort. Once this respiratory effort reaches a threshold level the patient will arouse and the muscles of the upper airway will reactivate thereby opening the pharyngeal airway. Ventilation then resumes and the hypoxia and hypercapnia are corrected. The individual then returns to sleep and the cycle begins again. The afflicted individual therefore cycles between apnoea and hyperpnoea, and also between sleep and wakefulness. Sleep is thus disrupted and the sequelae of hypoxia and hypercapnia ensue.

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