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EDITORIAL

Upper airway reflexes and obstructive sleep apnoea

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Reflexes originated from the supralaryngeal airways, larynx and lungs can affect upper airway calibre [1]. Specific receptors at the laryngeal level have been thought to be involved [2]. Nasal obstruction in normal men may cause apnoeas and in addition, more arousals and full awakenings from sleep [3]. The underlying mechanism remains unclear. It was demonstrated that nasal occlusion increases respiratory drive to the upper airways and that obstructive sleep apnoea is, therefore, not elicited by a decreased respiratory drive to upper airway muscles [4]. Apnoeas are likely to occur because increased airway resistance induces more negative airway pressures. It appears that "unknown" reflexes may be involved in the stimulation of upper airways (and in arousals).

Arterial chemoreflexes are known to provide a powerful excitatory input to inspiratory and expiratory hypoglossal motoneurons; their stimulation helps in maintaining upper airway patency [5]. It has even been postulated that peripheral chemoreceptor stimulation induced by hypoxia preferentially influences those motoneurons that regulate upper airway muscle activation [6]. However, recent data indicate that chemoreceptors do not affect upper airway muscle activity independently from other stimuli such as airway pressure [7].

Although reflex control may be important, it has also been demonstrated that dilatation of the upper airways is reflected by indices that quantify the central inspiratory drive in both normal subjects and patients with sleep apnoea [8]. This suggests that the activity of the central nervous system also plays an important role in the (in)stability of the upper airway.

Suppression of the reflexes originating in the upper airway by topical oropharyngeal anaesthesia leads to an increased number of obstructive apnoeas and hypopnoeas in normal men [9], confirming the possible clinical significance of these upper airway reflexes in maintaining patency of the upper airway during sleep.

In this issue of the journal, TOMORI *et al.* [10] have reviewed, in depth, a number of upper airway reflexes in the cat: including the sniff-like aspiration reflex and gasping. They describe the similarities and discrepancies between these two reflexes. Both reflexes are characterized by a powerful inspiratory effort. A fast and powerful activation of practically all phrenic motoneurons and inspiratory muscles occurs in both reflexes. Gasping reflexes after periods of severe anoxia do not have major clinical relevance. In contrast, aspiration reflexes that can be elicited by simple mechanical stimulation are very intriguing and of possible clinical interest if they also exist in humans. Such powerful activation of inspiratory muscles can only be of benefit in obstructive sleep apnoea, when upper airway activation is relatively greater than diaphragmatic stimulation. If this is not the case, obstructed breaths may well tend to increase.

RICHTER *et al.* [11–13] have demonstrated that the respiratory central pattern generator involves three phases, consisting of inspiration and two distinct periods of expiration, called post-inspiration (passive expiration) and stage II (active expiration). The post-inspiratory phase appears to mediate cessation of inspiration and is, therefore, affecting the respiratory rhythm. Mechanical or electrical stimulation of the upper airway can equally result in prolongation of the expiratory interval, when post-inspiratory mechanisms are involved and, therefore, provoke (severe) apnoea. Apart from timing, the type of stimulus may also be crucial.

In a study by LAWSON *et al.* [14], laryngeal insufflation with ammonia-saturated air, smoke and water was used in anaesthetized, paralysed and mechanically-ventilated piglets. This type of insufflation induced apnoea, during which stable membrane potentials were observed, in inspiratory and expiratory cells thus indicating that apnoea was provoked by post-inspiratory inhibitory mechanism.

During quiet sleep in tracheostomized infants, it was also shown that the effects of upper airway suction clearly depend on the timing of the stimulus. Application of the stimulus during early expiration clearly prolongs expiratory and inspiratory time of the stimulated breath. Application of the stimulus after the onset of inspiration shortens inspiratory and expiratory time of the same breath [15]. It therefore became clear that the timing of the stimulus is crucial, and that inconsistent results with various types of upper airway stimulation can be due to this phenomenon.

Why we do not try to elucidate "favourable" laryngeal reflexes such as the "aspiration" reflex to alleviate apnoeas? Clearly, this can only be successful if at the same time we try to avoid triggering the post-inspiratory inhibitory mechanisms.

In recent years, efforts have been made to evaluate the effects of electrical or mechanical stimulation of

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the upper airway. MIKI and co-workers [16, 17] demonstrated that percutaneous electrical submental stimulation decreases the incidence of apnoea episodes in patients with obstructive sleep apnoea. This type of stimulation mainly involves activation of the muscle itself, especially the genioglossus muscle. Other "reflex" stimulation cannot be completely ruled out. Reflex stimulation seems to be more clearly involved in increasing tonic and phasic EMG of the genioglossus, when oscillatory pressure stimuli are applied to the upper airway. When this was performed in subjects with sleep apnoea, the obstructed airway could be opened by applying the oscillatory stimulus. Electromyographic activity and respiratory response to high frequency oscillations are mediated by receptors in the upper airway [18–20]. Snorers may maintain patency of their airways by this mechanism. By eliminating snoring, treatment with continuous positive airway pressure could tend to suppress this type of reflex [21].

The aspiration-like reflexes elicitable by several types of stimuli (including pressure and mechanical stimuli) in animals, as illustrated in the work of TOMORI *et al.* [10], could equally well exist in humans and could be involved in the responses to, *e.g.* oscillatory pressures. It seems, therefore, attractive to develop and evaluate devices capable of dilating the upper airway by reflex mechanisms. Triggered application of pressure or mechanical stimuli can be used. We are looking forward to studies, in which these basic mechanisms are applied to the treatment of obstructive sleep apnoea in humans. In view of the large clinical spectrum of the sleep apnoea syndrome, these techniques could, at least, be applied to those obstructive sleep apnoea patients who do not accept or tolerate other more invasive treatment modalities, such as continuous positive airway pressure.

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