ACTA NEUROBIOL. EXP. 1973, 33: 329-341

Lecture delivered at Symposium "Neural control of breathing"
held in Warszawa, August 1971

THE ROLE OF PROPRIOCEPTIVE AFFERENTS IN THE CONTROL OF RESPIRATORY MUSCLES

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Abstract. Building largely on the results of previous studies of motor control in respiration the role of proprioceptive control of respiratory movements is discussed with particular reference to the significance of the following points: (i) The co-activation of fusimotor and alpha motoneurons in load compensation and in the control of velocity and force of the respiratory movements. (ii) The convergence onto the same intercostal spindle of fusimotor fibres for respiratory movements and for postural activity. (iii) The difference between proprioceptive control of intercostal muscles on the one hand and the diaphragm on the other, and of the control of the phrenic motoneuron pool exerted by intercostal proprioceptors. (iv) The cerebellar control both of the fusimotor-alpha balance between the indirect drive of the intercostal motoneurons and of the responsiveness of the phrenic motoneuron pool to respiratory and reflex influences. (v) Results suggesting spino-bulbar reflex effects on the control of rate and depth of respiration from muscle and joint receptors of the thoracic wall.

Since in anaesthetized and decerebrated animal preparations the respiratory muscles are the only ones which exhibit physiologically induced movements the mechanisms involved in the motor control of the respiratory muscles have provided a useful model for obtaining some understanding of the spinal mechanisms involved in the proprioceptive control of the various parameters of movements in general. As a matter of fact a great deal of our present knowledge of the spinal mechanisms involved in the control of aimed movements stems from investigations on the motor control in breathing. On the other hand most of our knowledge of muscle spindles, their receptor properties and centrifugal control by their fusimotor innervation as well as of their role in the control of posture comes from studies on the limb muscles. The extensive work of Lennerstrand (1968) has provided the comparisons of the dynamic muscle spindle properties in the antigravity muscles of the hind legs and the intercostal muscles which permit a mutually beneficial use of the knowledge acquired about the different motor systems.

Much of the work on the proprioceptors of the intercostal muscles and the diaphragm, the supraspinal fusimotor control of the muscle spindles of the respiratory muscles and the spinal mechanisms involved in the proprioceptive control in breathing has been summarized earlier (e.g. Sears 1964, 1966, Euler 1966*ab,* 1970; *see also* Granit 1970). In this presentation I shall drew attention to only a few points which may be of special interest at this conference.

Much of the discussion concerning proprioceptive control in breathing has centered around the problem of "load compensation", a term coined to emphasize a functional aspect of the fusimotor-muscle spindle circuit in the control of movements, as opposite to posture or antigravity control. In principle, the myotatic load compensation is similar to the classical stretch reflex in that a hindered shortening in contraction, provoked by some increased loading of the moving system, causes a relative increase in afferent discharge from the muscle spindles and consequently a corresponding increase in the motoneuron output to the extrafusal muscles leading, in turn, to increased force of contraction and thus opposing the effect of the imposed load. This type of load compensation by excitatory feed back of afferent information from the muscle spindles to the motoneurons requires a fairly strong co-activation of fusimotor and alpha motoneurons. The much discussed follow-up length servo (Hammond et al. 1956) is certainly in operation in respiratory motor control as evidenced by the commonly occurring increase of spindle discharge during the phase of contraction (Critchlow and Euler 1963), but a direct supraspinal activation of the alpha motoneurons seems always to occur in addition to the excitation by the round about rout over the fusimotor-muscle spindle servo (Euler 1966*a,* 1970). An exclusive driving of alpha motoneurons by the follow-up length servo has not been convincingly demonstrated anywhere in the mammalian motor system, for that matter (*see* Granit 1970). The capability of the fusimotor-muscle spindle system to drive the alpha motoneurons all by itself has, however, been clearly demonstrated (Granit et al. 1966). The load compensation by the fusimotor-muscle spindle system is virtually an inevitable consequence of a strong and precise fusimotor-alpha co-activation — which has been well established in the respiratory motor system, at least in the cat. The presence in man of myotatic load compensation is made likely by electromyographical studies (Sears and Newsom Davis 1968, Newsom

Davis and Sears 1970) although in experiments on human subjects it would seem difficult to exclude the possibility of vagal reflexes both from the lungs and from the upper airways. There seems to be accumulating evidence indicating that the vagal inflation reflex is of functional significance also in man (Guz et al. 1970, Guz and Trenchard 1971, Guz and Widdicombe 1970, Clark and Euler 1970, 1972). It should be recalled that also the pulmonary stretch receptors and the vagal nerves form part of a potent load compensating mechanism. If the vagal nerves are left intact an increase in efferent inspiratory activity, as recorded in branches of the intercostal nerves, is regularly obtained in response to an imposed airway restriction or a loading of the chest wall also when the fusimotor-muscle spindle loop had been blocked, for example by gallamine. The vagal load compensation, however, involves not only the intercostal muscles but also the diaphragm. The diaphragm, it is recalled, has a scanty supply of muscle spindles and exhibits no sign of load compensation after bilateral vagotomy (Corda et al. 1965*ab*).

The enhancement of inspiratory activity in response to an imposed hindrance of the inspiratory movement is thus, at least in the cat, more efficiently achieved by the vagal route, governed by the inflation receptors, since this control circuit involves also the diaphragm. It should be emphasized, however, that there is an important difference between the myotatic and the vagal response to an imposed load. Whereas the former mechanism causes an increased rate of increase in the inspiratory activity with a latency of about 40–60 msec, the vagal mechanism, governed by the inflation receptors, does not cause any significant change in the initial time course of the rate of increase and recruitment of inspiratory activity. The vagal mechanism works mainly by means of prolonging the duration of the inspiration (e.g. Head 1889, Larrabee and Knowlton 1946, Euler et al. 1970, Clark and Euler 1972) allowing the inspiratory activity to climb to higher final values then for the unrestrained shorter inspirations. Since only the vagal load compensation (but not the myotatic one) incorporates the chief inspiratory muscle, the diaphragm, it does not seem likely that the main functional significance of the fusimotor-muscle spindle control system is to compensate for such added loads which exert a mechanical impedence to the breathing movements (Euler 1966*b*, 1970). This conclusion is further supported by the finding that reflex inhibition is also at play at the segmental level, the more the larger the chest volume (Fig. 1).

The myotatic servo may also be subjected to other types of loading or equivalent disturbances, e.g. in the form of selective changes in the input to the alpha motoneurons without concommitant activation of the fusimotors. The myotatic control circuit, with an optimal balance of

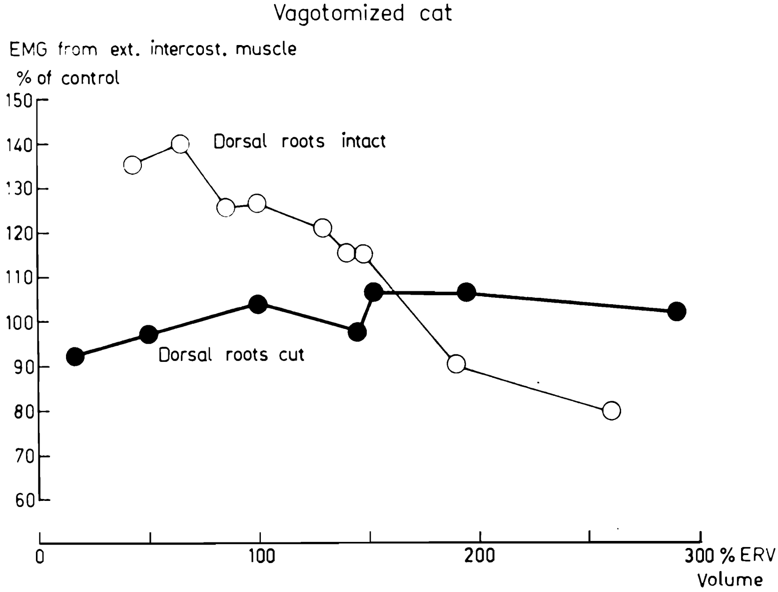

Fig. 1. Relation of lung volume to 'integrated' inspiratory external intercostal EMG in a vagotomized decerebrate cat. Each point represents average 'integrated' inspiratory activity during tracheal occlusion as a percentage of the activity during unrestrained breaths. Open circles before and filled circles after cutting the dorsal roots from C_3 to T_{12}. The Figure shows that with intact dorsal roots the electrical activity decreased with increasing thoracic volume. After cutting the dorsal roots the expansion of the chest wall no longer influenced the electrical activity. Nor did clamping the trachea influence the electromyogram as it did when the dorsal roots were intact. Thus the dorsal roots reflexively enhanced the motoneuron activity at small and moderate thoracic volumes and inhibited the activity at large volumes. The activity equaled that of unobstructed inspiration (100%) at a volume of about 150% ERV, the point reached at the peak of the unrestricted tidal volume. (From Euler and Fritts 1963).

the fusimotor-alpha co-activation, would treat neural inputs reaching the alpha motoneurons alone as disturbances and outregulate them to the same extent as disturbances in the form of externally applied loads. This implies that, in order to be effective in controlling the efferent output to the muscles and thus the contractile force of the muscles, input control signals to the motoneuron pool have to be funnelled not only to the alpha motoneurons but also to the fusimotor neurons or to the latter alone (Euler 1970).

A load compensating effect of a completely different kind resides in the contractile properties of the muscle fibres themselves and has nothing to do with reflex control. This is the well known force-length relation of innervated skeletal muscle according to which the tension developed by a certain constant efferent activation is proportional to the extension of the muscle. A load-preventing shortening in contraction will thus prevent the contractile force from decreasing. From another point of view, however, the decrease in force exerted by the muscle as it shortens may in itself be regarded as a progressively increasing loading of the system called upon to execute a certain length change. This would require a compensatory increase in efferent activation of the muscle to ascertain the necessary force. Muscle spindles activated in a tight fusimotor-alpha co-activation will inevitably produce effects in this direction. The tendon organs, by the decreasing inhibition they exert on the alpha motoneurons as the force gets weaker, will cause a seemingly similar stabilizing effect; the diaphragm, it should be recalled, has a relatively richer innervation with tendon organs than with muscle spindles (Corda et al. 1965*b*).

The fairly linear length-tension relation referred to above is basically a static relationship between contractile force and extension. If we take the rate of shortening into account, as we certainly should also when discussing respiratory movements (Agostoni and Fenn 1960, Hyatt and Flath 1966, Nattie and Tenney 1970) the requirement for compensatory

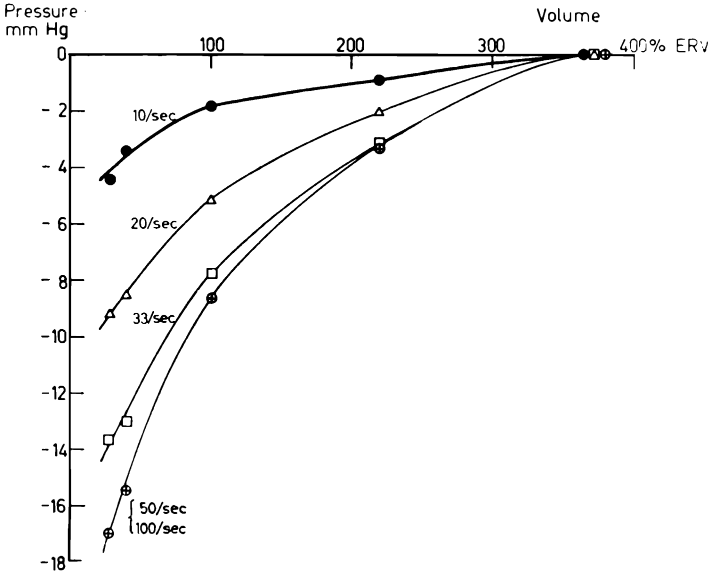

Fig. 2. Pressure-volume relationship of the respiratory system in cat (Dial anaesthesia) during tetanic stimulation of both phrenic nerves at different rates of stimulation. The decrease of the exerted pressure with increasing volume depends on two factors: (i) the force-length relation of the muscle fibres and (ii) the decreasing fraction of the muscle force which can exert an intrathoracic pressure as the direction of the muscle force changes with lung volume (C. von Euler and H. W. Fritts, unpublished data.)

changes in efferent alpha innervation may be even bigger. The slow motor units in a muscle are regularly recruited early in a motor act, the faster units being saved for later recruitment. This is the case also in intercostals (Corda et al. 1966, Cugell and Euler 1969) and in the diaphragm (Decima and Euler 1969*a*, Yaşargil 1967). The slow muscle fibres, however, can develop relatively little force during acceleration (Fig. 3), but their unability to do so is probably felt by the fusimotor activated spindles which, on excitation, are able to recruit new faster motor units (Corda et al. 1965*a*) with greater ability to carry a load during acceleration (*see* Granit 1970). However, the role of muscle spindles with fusimotor and alpha co-activation in the control of velocity is still almost entirely a matter of guessing. Anyhow it would probably work only for the intercostals since the diaphragm has a scanty supply of muscle spindles. The pronounced difference in proprioceptive control of the intercostal muscles on the one hand and the diaphragm on the other, strongly suggests that the functional significance of the fusimotor-muscle spindle control system of the intercostal musculature is related to the regulation against other types of load or 'disturbances' than merely mechanical resistance to shortening of the muscles during contraction, e.g. imposed airway resistances, external loading of the ribcage or contraction of antagonists. The demonstration in our laboratory of a convergence of fusimotor fibres belonging to two functionally different systems, (i) those involved in the control of the respiratory movements and (ii) those involved in the control of postural function of the intercostal muscles (Massion et al. 1960), converge onto the same muscle spindles (Corda et al. 1966) suggests that perhaps most important function of the proprioceptive control mechanisms of the intercostal musculature is to integrate the demands for respiratory movements on the one hand and movements

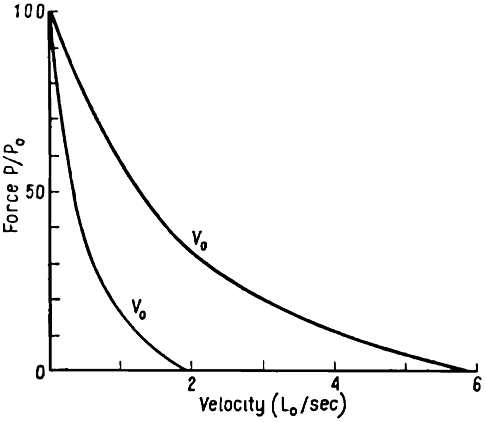

Fig. 3. Diagrams relating force and shortening velocity of fast and slow muscle in rat. The curve in heavy line is derived from the fast anterior tibial muscle and the fine line from the slow soleus muscle. L_0, standard length of muscle; P, muscle tension and P_0, maximal muscle tension at standard length. (From Wells 1965.)

and posture of the trunk on the other, one function exerting a kind of loading on the other. The diaphragm does not seem to require a mechanism for such integration; its role in movements and postural changes is probably small.

The absence of evident autogenetic facilitatory proprioceptive reflex effects on the phrenic motoneurons (Gill and Kuno 1963, Corda et al. 1965*b*) appears to be compensated for, to some extent at least, by the existence of powerful intercostal-to-phrenic reflexes (Garcia Ramos and López Mendoza 1959, Decima et al. 1969, Decima and Euler 1969*ab*, Remmers 1970), the facilitatory aspects of which were found to be limited mainly to the lower intercostals. Neural control circuits have thus been found to govern the tight mechanical linkage between the diaphragm and the ribcage whereby the contracting diaphragm, in addition to its descending movement is able to lift the lower ribs in a rostral direction using the abdominal viscera as a fulcrum, and so expand the lower thoracic aperture. This neural reflex control is complex and has both facilitatory as well as inhibitory components. Proprioceptive control under the supervision of the cerebellum seems thus to be called upon to adjust for the loading and unloading effects that the intercostals and the diaphragm mutually exert on each other in breathing and in postural movements.

In summary, at segmental levels the proprioceptive control of the respiratory muscles seems to be involved in adjustments of the force of

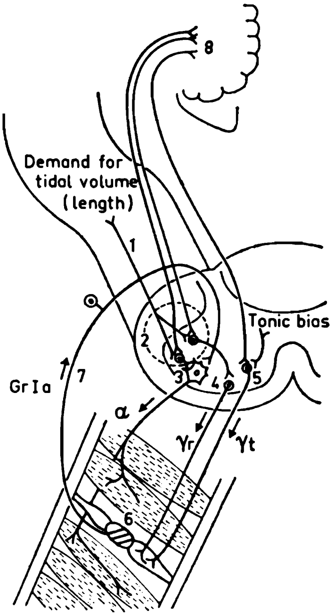

Fig. 4. Schematic representation of an external intercostal muscle, its myotatic loop and some of its supraspinal control paths. *1*: Bulbo-spinal respiratory path transmitting the descending demand information to spinal levels. *2*: The alpha-gamma 'linkage' from where the central respiratory instructions are channeled *via* interneurons to both the alpha (*3*) and the 'rhythmic' gamma motoneurons (*4*; γ_r). The balance of the α-γ_r linkage can be adjusted from cerebellum (*8*). *5*: 'Tonic' gamma motoneurons (γ_t) are influenced both from spinal inputs and from cerebellum. *6*: Muscle spindle primary ending with its Gr Ia afferent (*7*) and innervated both by a 'rhythmic' (γ_r) and a 'tonic' (γ_t) fibre representing the multineuronal fusimotor innervation of spindles. (From Euler 1970.)

contraction to meet various kinds of loads subjected to the system, both externally applied and those imposed by changes in the balance between the demands for respiration and for movements and posture of the trunk. Proprioceptive control at segmental levels is possibly also involved in the adjustment of the motor output to meet the requirements at different lengths of the muscle and at different velocities of muscle shortening. Proprioceptive control at spinal level is also involved in the neural coordination between the different intercostal muscles and between intercostals and the diaphragm.

Although our understanding of the segmental reflex mechanisms is very limited we know far less about ascending proprioceptive information from the respiratory muscles and the ribcage to supraspinal levels and about the possible role of such information in the regulation of breathing. Gesell, Magee and Bricker (1939) recorded respiratory activity in the dorsal column nuclei of the dog. Yamamoto, Shigihara and Kuru (1956) likewise recorded afferent respiratory activity in the posterior funicullus of the cat, and Euler and Söderberg (1952) found afferent respiratory activity in the bulbar reticular formation.

A facilitatory effect on breathing has been reported for dogs, cats and rabbits following the application of pressure round the thorax (Bakos and Howell 1948, Culver and Rahn 1952), an effect which commonly has been employed to maintain adequate ventilation in rabbits under pentobarbitone anaesthesia. This effect was reported to be completely abolished after bilateral vagotomy, however. Remmers (1970), on the other hand, has studied inhibitory aspects of the intercostal-to-phrenic reflexes which could be elicited from the mid-thoracic region and which seemed to be mediated by supraspinal structures. In recent studies on problems concerning the regulation of depth and rate of breathing Clark and Euler (1972) have found that the characteristics of the volume threshold for the termination of inspiration mediated by the vagus nerves (Hering–Breuer threshold) were not significantly different in three types of cat preparation: (i) spontaneously breathing animals in which depth and duration of active breaths were altered by different levels of end-tidal CO_2%, (ii) animals in which the volume threshold was assessed by pulses of passive, artificial inflations superimposed on spontaneous inspirations and (iii) animals paralyzed with gallamine and tested for the Hering–Breuer threshold with pulses of passive inflations. For the latter group it can be concluded that the proprioceptive input from both tendon organs and muscle spindles is much altered by the neuro-muscular paralysis which, with the doses used, befalls on both extra- and intrafusal muscles. In both the non-paralyzed and the paralyzed animals we found no significant changes in phrenic activity at subthreshold inflations or before the imposed inflation had reached the threshold for termination of inspiration when the phrenic activity was cut off. These findings do not leave much room for afferent information from the chest wall to exert similar effects on the pattern of breathing as those mediated by the vagus nerves. The recent report by Camporesi and Sant'Ambrogio (1971), however, seems to be of considerable significance in this respect. Working with rabbits they applied the method of Decima et al. (1969) to produce a pull on the lower ribs and intercostals by jerks of the diaphragm elicited, in turn, by short tetanic stimulation to the peripheral end of the cut phrenic nerves. After bilateral vagotomy a sudden jerk of the diaphragm, applied in the phase of expiration, regularly caused a significant shortening of the expiratory phase, an effect which was abolished by spinal transection at the level of T_I. In contrast, with intact vagi brief inflations evoked by phrenic stimulation during the expiratory phase produced the classical effect of prolongation of the expiratory phase.

Another recent approach that offers the promise of revealing new information in this respect comes from some observations on respiratory complications in patients who have undergone cervical cordotomy for pain relief. Unilateral cordotomy in man has been reported to result in a significant reduction of tidal volume together with a significant increase of respiratory rate with little or no change of minute ventilation (both on room air and on 5% CO_2) nor of vital capacity, respiratory muscle strength or regularity of breathing (Rosmoff et al. 1969). Later studies on cats have suggested that the signs developed by cordotomy lesions may include impairment of an afferent system converging onto the vagal inspiration-inhibition mechanism (Christensen et al. 1969, Krieger et al. 1969).

We thus have to admit that, on the whole, very little is known about proprioceptive information ascending from the chest walls to supraspinal levels. My own attitude towards the many negative and the few, and rather vague, positive results in this respect is definitely not one of scepticism against the importance of such ascending information. On the contrary I feel that we just have not yet learned the tricks to reveal its functional significance in feedback control of the respiratory movements. Recent work by Coffey, Godwin-Austen, MacGillivray and Sears (1969) will again direct attention to the cerebellum. Recent work in our laboratory has shown that cerebellar stimulation can induce (i) shifts in the balance of the fusimotor-alpha co-activation — in the intercostal myotatic servo (Corda et al. 1966, *see* Granit et al. 1955, Granit 1970), and (ii) control of the responsiveness of the phrenic motor pool both to the respiratory drive and to the reflex influence from the lower intercostals (Decima and Euler 1969*b*). This suggests that an important role of the

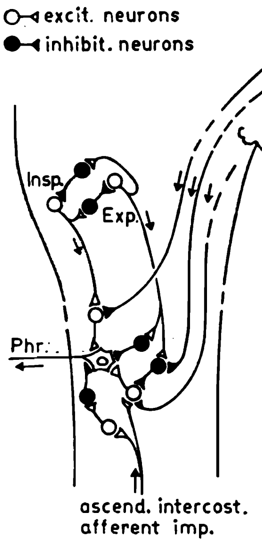

Fig. 5. A schematic representation of some features of the cerebellar control of the phrenic motoneurone pool. In this hypothetical diagram inhibitory functions has only been represented by postsynaptic mechanisms. Insp. and exp. represent the reciprocally occurring inspiratory and expiratory activity descending from the respiratory mechanisms in medulla. The pathways from cerebellum are broken to indicate that they might be interrupted by brain-stem relays. (From Decima and Euler 1969b.)

ascending information from the chest wall may be found in the area of cerebellar control of the respiratory muscles especially for a differentiated amplitude control of the different muscles and for the integration of respiratory activity with postural activity and voluntary movements of the trunk (Moruzzi 1940, Meulders et al. 1960), i.e. in the same area where the muscle spindles seem to play a major role at the segmental level.

This investigation was partially supported by the Swedish Medical Research Council (Project 14X-544).

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