

SPINAL INTEGRATION OF SEGMENTAL, CORTICAL AND BREATHING INPUTS TO THORACIC RESPIRATORY MOTONEURONES

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SUMMARY

1. The spinal integration of cortical, segmental and breathing inputs to thoracic motoneurons was studied in anaesthetized, paralysed cats: the breathing input was intensified by underventilation or abolished by hyperventilation.

2. In apnoeic animals, low intensity stimulation of an internal intercostal nerve evoked a brief latency polysynaptic reflex discharge of expiratory motoneurons (direct response) in several adjacent segments with no or little response of the inspiratory motoneurons.

3. A similar direct response of expiratory motoneurons occurred with brief tetanic stimulation of the trunk area in the contralateral sensorimotor cortex.

4. Conditioning of an intercostal-intercostal test reflex by a prior stimulus to an intercostal nerve or to the cortex gave conditioning curves showing facilitation of transmission to expiratory motoneurons at short intervals (5-25 msec) and inhibition at long intervals (25-200 msec).

5. The direct response of expiratory motoneurons to the cortical or segmental inputs was depressed during the inspiratory phase when the animal was underventilated; conversely the spontaneous activity of the inspiratory motoneurons was inhibited for a period that corresponded with the direct response or to the phase of facilitated transmission to expiratory motoneurons. During the expiratory phase, the cortically or segmentally induced direct response was facilitated but the inhibition of inspiratory motoneurone activity was concealed by the absence of spontaneous activity.

6. It was possible with discrete lesions of the spinal cord to differentiate between the pathways subserving the responses to cortical stimulation and the spontaneous activity due to the breathing input.

7. To account for the results a working hypothesis is proposed utilizing

a segmental interneuronal network which transmits mutual reciprocal inhibition between inspiratory and expiratory motoneurones.

INTRODUCTION

During spontaneous breathing, thoracic motoneurones show rhythmic changes in membrane potential, the central respiratory drive potentials (CRDPs), which are due to alternating excitatory and inhibitory synaptic drives distributed reciprocally to inspiratory and expiratory motoneurones (Eccles, Sears & Shealy, 1962; Sears, 1964*d*). These synaptic drives, which are of supraspinal origin, show an interdependence in which increased excitation of inspiratory motoneurones is associated with a greater inhibition of expiratory motoneurones and vice versa. This suggests that a spinal network of interneurones might subservise the reciprocal activation of inspiratory and expiratory motoneurones. A similar network has been postulated to underlie the excitation of inspiratory motoneurones with reciprocal inhibition of expiratory motoneurones which follows stimulation of reticulospinal fibres (Anderson & Sears, 1970) and the converse reciprocal effects which occur with stimulation in the pyramidal decussation (Sears, 1966). In the present study we have investigated the spinal integration of the reciprocal activities of inspiratory and expiratory motoneurones evoked by cortical and segmental inputs with the reciprocal activities which occur during spontaneous breathing. A preliminary account of this work has already appeared (Aminoff & Sears, 1970).

METHODS

The experiments were performed on twenty-two cats anaesthetized with sodium pentobarbitone (initial dose 35 mg/kg *i.p.*, with *i.v.* supplements of 3.0–5.0 mg/kg as required). In most experiments the cats were paralysed with gallamine triethiodide and maintained on positive pressure artificial ventilation. The dissection and nomenclature of the intercostal nerves and the general fixation of the preparation are described in previous papers (Sears, 1964*a, b*). By monitoring efferent discharges (inspiratory) from an external intercostal nerve, usually in the mid-thoracic region (T4–T7), the spontaneous respiratory activity could be maintained at any required level or abolished altogether by altering the level of ventilation. Body temperature was maintained between 36 and 38° C by means of a heating pad.

For segmental reflex activation of the thoracic motoneurones the central end of an internal intercostal nerve was stimulated and the reflex discharge recorded monophasically from adjacent intercostal nerves as described by Downman (1955). The stimulating and recording electrodes were usually sited at the angle of the ribs. With this reflex, motoneurones discharge asynchronously because of transmission through a polysynaptic pathway. To provide an estimate of motoneurone excitability the area of the monophasic reflex discharge was measured by electronic integration using an operational amplifier with capacitive feed-back. The period of integration was adjustable over any selected phase of the response ('gated integration') by

controlling the integrator 'reset' through the gate pulse from a Digitimer (Devices Sales Ltd).

The contralateral sensorimotor cortex was exposed for stimulation and protected from drying by a paraffin pool formed by elevating the skin flaps. A unipolar spring-mounted silver ball electrode was used as a stimulating cathode and the anode was a silver plate applied to the moist frontal skin flap. The stimuli were brief trains (usually three shocks) of rectangular pulses, 0.2 msec duration, 500 Hz from an isolated stimulator (Devices Sales Ltd).

Stimulation was carried out mainly in the trunk area of the cortex which was delineated in each experiment by observing the nature and distribution of the movements evoked by threshold cortical stimulation before paralyzing the animal. The movements consisted of retraction at the contralateral shoulder with brief contractions of the abdominal and thoracic musculature at optimal sites of stimulation, the most effective area being posterior to the cruciate sulcus midway between the dimple and ansate sulcus (Fig. 4).

Discrete lesions of the spinal cord were made with scissors or fine forceps and combined with suction through a small pipette. The extent of the lesions was confirmed histologically using paraffin sections stained with haematoxylin and eosin.

RESULTS

These experiments deal with the general characteristics and interaction between the responses of thoracic motoneurons to three different inputs, segmental, cortical and that which we refer to as the 'breathing input', namely the synaptic drives generating the CRDPs. First, we describe the independent responses to, and the interaction between, segmental and cortical inputs in paralysed animals which have been made apnoeic by mechanical hyperventilation; secondly we describe their interaction with that of the breathing input when the animal is hypoventilated.

Segmental input in apnoea

During spontaneous breathing the electroneurogram of the external intercostal nerves in the upper and mid-thoracic regions invariably showed rhythmic discharges during inspiration (cf. Sears, 1964*b*). This activity was abolished in the paralysed animal by adjusting the level of artificial ventilation so that, on stopping the pump, the ensuing apnoea in the electroneurogram lasted for at least 15 sec.

Stimulation of the cut central end of an internal intercostal nerve evoked an asynchronous discharge in adjacent intercostal nerves due to reflex transmission in polysynaptic pathways (Downman, 1955). When this reflex was evoked with simultaneous recording from the internal and external intercostal nerves, thus monitoring the activity of expiratory and inspiratory motoneurons respectively, we found that with moderate stimulus intensities the reflex discharge occurred predominantly, if not exclusively, in the expiratory motoneurons (Fig. 1 and Figs. 2, 5 and 7). The latency of this response, when evoked from an immediately adjacent

segment (see Methods) was approximately 5.0 msec. If the inspiratory motoneurons responded, as they could with strong stimulation, it was with a longer latency than that of expiratory motoneurons such that the onset of their brief discharge coincided with the offset of the reflex discharge of expiratory motoneurons. This selective reflex activation of expiratory motoneurons was best seen with stimuli giving submaximal reflex excitation. The mean threshold for the polysynaptic reflex is approximately 2.0 times nerve threshold and it is obtained usually with excitation of the Group 1 'c' and highest threshold Group 1 'b' components of the internal intercostal afferent volley recorded from the cord dorsum (Sears, 1964c). Whereas low intensity stimulation of the cutaneous division of the lateral intercostal nerve caused a similar reflex discharge, stimulation of the muscle nerve to the external intercostal muscle was usually without effect unless much higher stimulus intensities were used when a weak discharge of the expiratory motoneurons could occur. In the experiment illustrated in Fig. 1 low intensity stimulation also evoked a brief latency (2.0 msec) response clearly separated from the main reflex response which had an unusually low threshold at 1.5 times nerve threshold. In the intercostal nerves the lowest threshold afferent fibres, which cause the 1 'a' component of the cord dorsum potential, distribute monosynaptic excitation to expiratory motoneurons of the same and adjacent segments (Sears, 1964c); excitation of these fibres would account for the early response.

The intercostal-to-intercostal reflex was further characterized by the manner in which it was conditioned by a weak preceding volley which did not itself evoke a reflex discharge. The curve in Fig. 2 is typical of the ten obtained from six cats. It demonstrates that the initial effect of a conditioning volley in the same nerve is facilitation maximal between 2.0 and 6.0 msec, followed by an inhibitory phase maximal between 40 and 60 msec, and declining over the following 100 msec. The duration of the facilitatory phase, which has varied between 18 and 30 msec in different experiments, seems mainly to be dependent on the degree of inhibition present and the latency of its onset. Thus on one occasion a typical facilitatory-inhibitory conditioning curve was subsequently transformed by a spontaneous loss of the inhibitory phase to a curve which showed only a phase of prolonged facilitation. This suggests that the conditioning curve represents summation between overlapping excitatory and inhibitory processes.

Cortical input in apnoea

Stimulation of fibres in the pyramidal decussation evokes a pronounced excitation of expiratory motoneurons with reciprocal inhibition of inspiratory motoneurons (Sears, 1966). We therefore attempted to obtain

such reciprocal activity by stimulating different areas of the cerebral cortex. A preliminary survey revealed that a direct response of expiratory motoneurons as illustrated in Fig. 3 could be evoked from the contralateral sensorimotor cortex around the area defined by the post-cruciate dimple anteriorly and the ansate sulcus posteriorly (inset diagram, Fig. 4). This direct response closely resembled the reflex response to a segmental

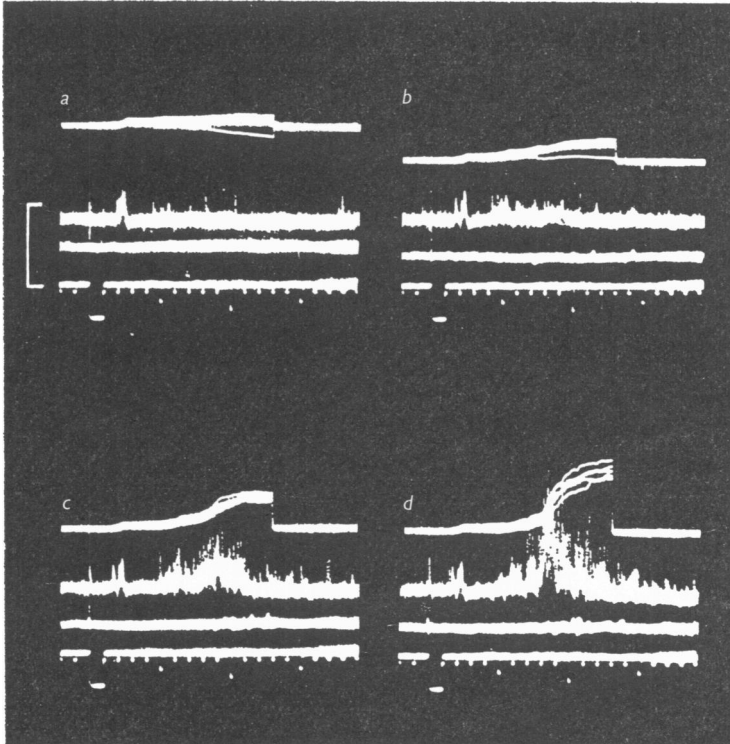


Fig. 1. Response of thoracic expiratory and inspiratory motoneurons to a segmental input. Internal intercostal nerve T9 stimulated. From above down: integral of response in internal intercostal nerve T8; response from internal intercostal nerve, T8; response from external intercostal nerve, T8; time scale 1.0 msec; vert. cal. 100 μ V. *a-d*, 1.5, 3.0, 6.0 and 10.0 times nerve threshold.

input and consisted of a compact but asynchronous discharge of expiratory motoneurons with a latency which ranged from 5 to 8 msec, for example, at the eighth thoracic segment.

Even with surface stimulation within the area defined above, there appeared to be circumscribed regions from which responses in a given intercostal nerve could be obtained more readily, either at lower intensities or with fewer shocks (Fig. 3*d, e* and *f*). Using threshold stimulation at such sites, moving the ball electrode no more than its diameter (0.6 mm) could

result in loss of the response in a segment or its appearance in another (Fig. 3*a, b*). In the following account the stimulating cathode was placed on such a specific cortical site. Apart from stimulus intensity, the magnitude of the response was determined by the polarity of the stimulating electrode, surface cathode being the more effective (Fig. 3*h, i*) and by the number of shocks applied. A brief train of 3–4 shocks at 500 Hz was the most effective in evoking a direct response, additional shocks simply prolonging the duration of the discharge (Fig. 3*c–g*).

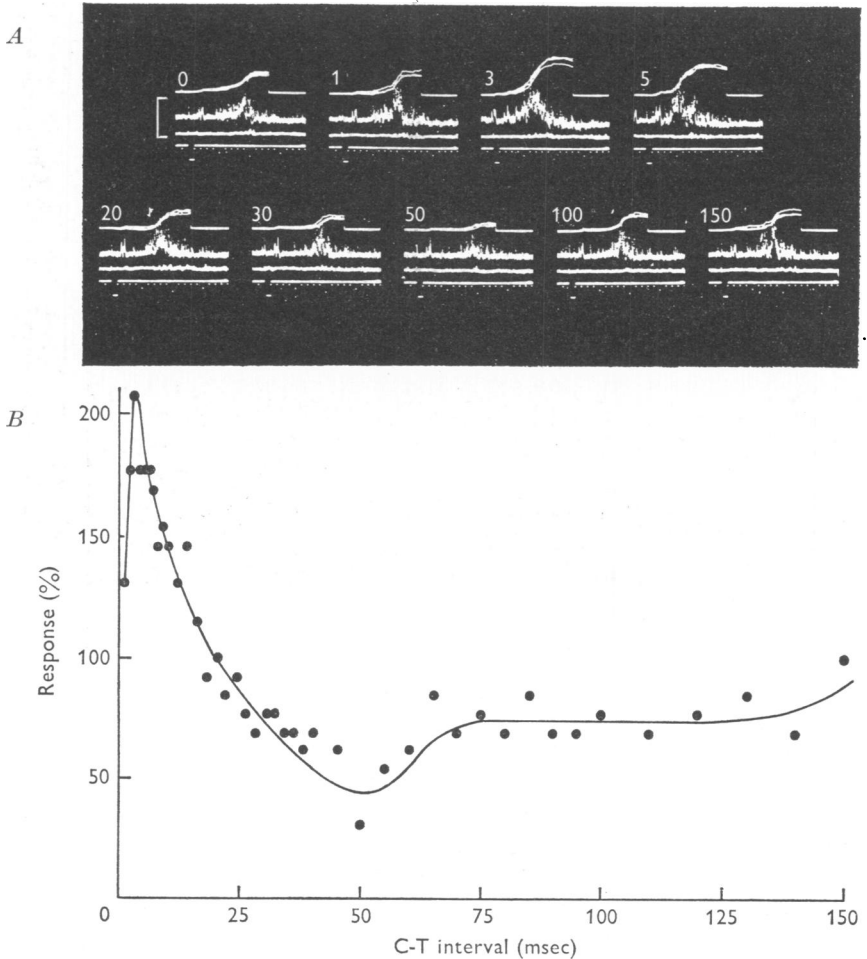


Fig. 2. Intercostal conditioning of an intercostal test reflex. Conditioning volley subliminal for reflex activation. Stimulation and recording as in Fig. 1. *A*, sample records at the conditioning intervals indicated above in msec, with control at 0. *B*, conditioning curve; ordinate, integral of the response plotted as % control (each point average of three responses); abscissa interval between conditioning and test stimuli in msec.

When a cortical stimulus, itself subliminal for a direct response, preceded an intercostal-to-intercostal test reflex, the general time course of the resulting conditioning curve was similar to that obtained with conditioning by a weak intercostal volley (Fig. 4). Essentially similar curves were obtained from experiments in fifteen cats, with facilitation at short intervals (5–10 msec) and inhibition maximal between 40 and 60 msec.

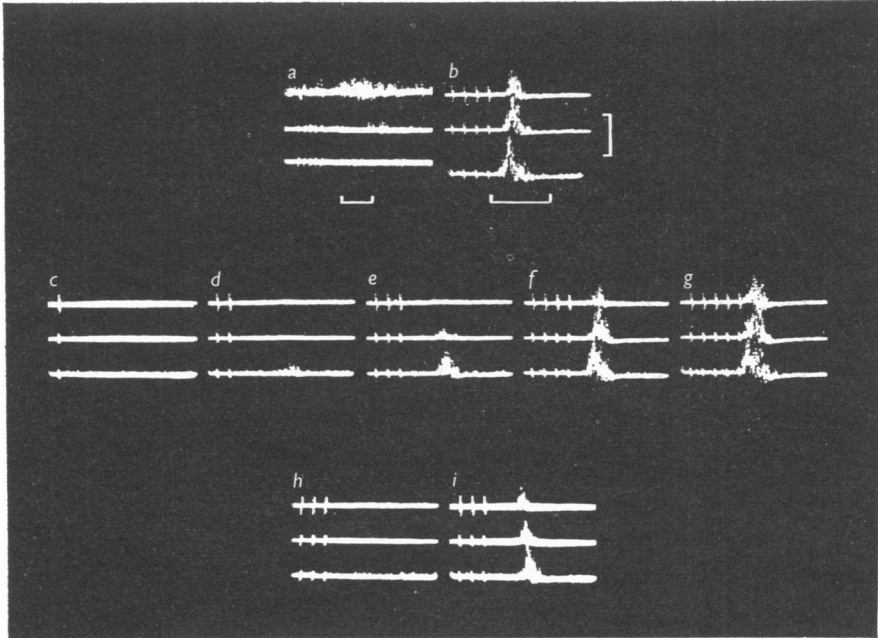


Fig. 3. Response of expiratory motoneurons to cortical stimulation. Upper, middle and lower traces, recordings from internal intercostal nerves, T4, 6 and 8 respectively. Horizontal bar 10 msec; time scale for *c-i*, same as *b*; vertical calibration, 100 μ V.

a and *b*, responses to stimulation at sites 0.6 mm apart; *c-g*, effect of increasing the number of shocks in a brief tetanus; *h*, surface anodal and *i*, surface cathodal stimulation of cerebral cortex.

As with intercostal conditioning, facilitation present at extremely short intervals between conditioning and test shocks (cf. Fig. 2) was due both to the long central delay of the test reflex and to the manner in which facilitation of late components of the test reflex contributed to the total integral.

Interaction of segmental and cortical inputs with the breathing input

In this series of experiments, mechanical ventilation was maintained at a level which restored an effective breathing input to the motoneurons as indicated by the resumption of spontaneous, rhythmic discharges (in-

spiratory) in the external intercostal nerves of the upper and mid-thoracic regions.

The response of the inspiratory and expiratory motoneurons to both the segmental and cortical inputs was now profoundly affected by the phase of the respiratory cycle. When either an internal intercostal nerve

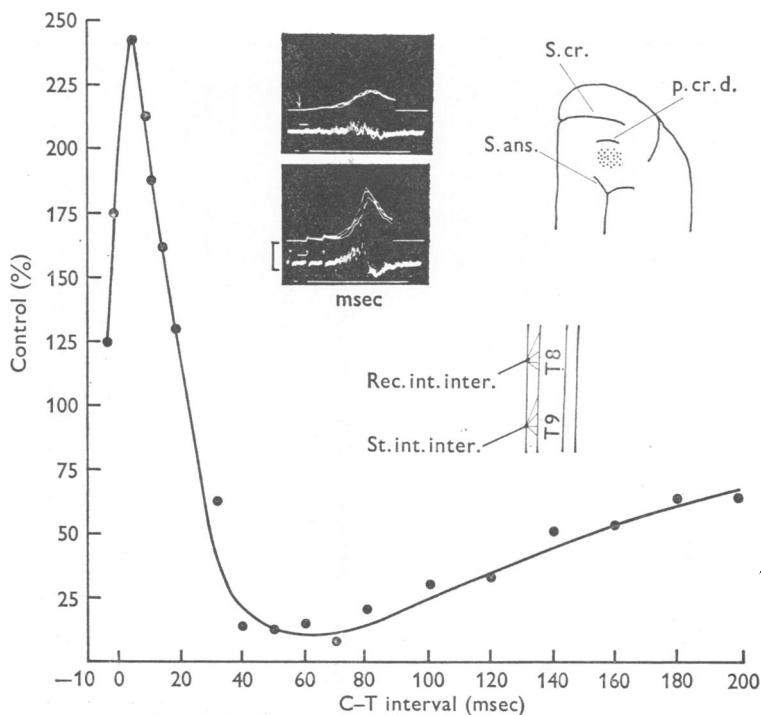


Fig. 4. Cortical conditioning of intercostal test reflex. Stim. Internal intercostal nerve, T9. Rec. Internal intercostal nerve, T8. Ordinate, integral of response plotted as % control (average of three responses); abscissa, interval between cortical conditioning stimulus and test stimulus (C-T interval) in msec. Conditioning volley: three shocks, 500 Hz, surface cathode. Of the two sample records the upper is of an unconditioned control test reflex, the lower of the reflex cortically conditioned 1 msec before the test shock. Upper trace in each record, integral of, and lower trace response in internal intercostal nerve, T8. Inset diagram shows stimulating and recording arrangements; stippled cortical area indicates lowest threshold sites of stimulation for direct response. S.cr., cruciate sulcus; p.cr.d., post-cruciate dimple; S.ans., ansate sulcus.

or the cerebral cortex was stimulated during the inspiratory phase, a direct discharge of expiratory motoneurons was evoked, as before; but this was now accompanied by a striking reciprocal inhibition of the inspiratory activity in the same and neighbouring segments (Figs. 5-8). This inhibition was of both fusimotor and alpha motoneurone activity. The upper pair of

traces in Fig. 5 is a control showing superimposed sweeps in mid-inspiration with discharges in the inspiratory nerve filling the entire trace (ext. T6). The lower trace of the middle pair shows the direct response of expiratory motoneurons (int. T8) to an intercostal test shock applied in mid-inspiration. This is now accompanied by reciprocal inhibition of the

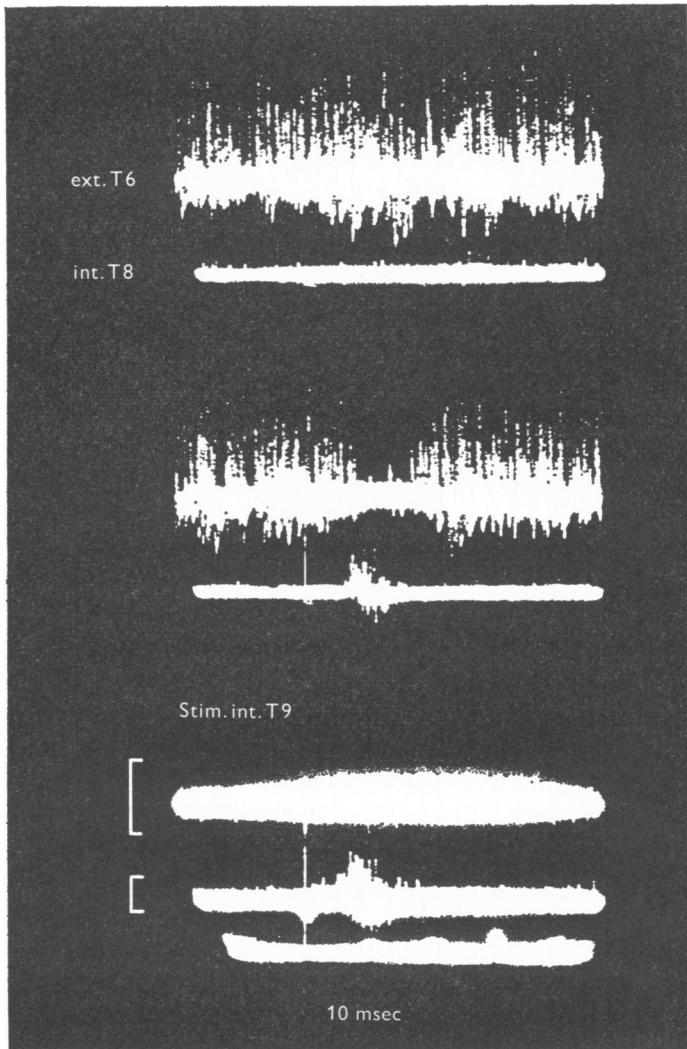


Fig. 5. Interaction between breathing and segmental inputs. In each pair of recordings, upper trace from external (T6), lower trace from internal (T8) intercostal nerves. Each record shows five superimposed sweeps repeating at 6/sec. Vertical calibration $100 \mu\text{V}$. Time marker 10 msec. Control records in mid-inspiration (upper pair); stimulation of internal intercostal nerve (T9) in mid-inspiration (middle pair) and mid-expiration (lower pair).

spontaneous inspiratory activity; characteristically the duration of the inhibition is longer than that of the direct response. The lowermost pair of traces shows the response to the same test shock applied in mid-expiration; neither spontaneous nor reflexly evoked activity of the inspiratory motoneurons occurs, but the direct response of the expiratory motoneurons is enhanced.

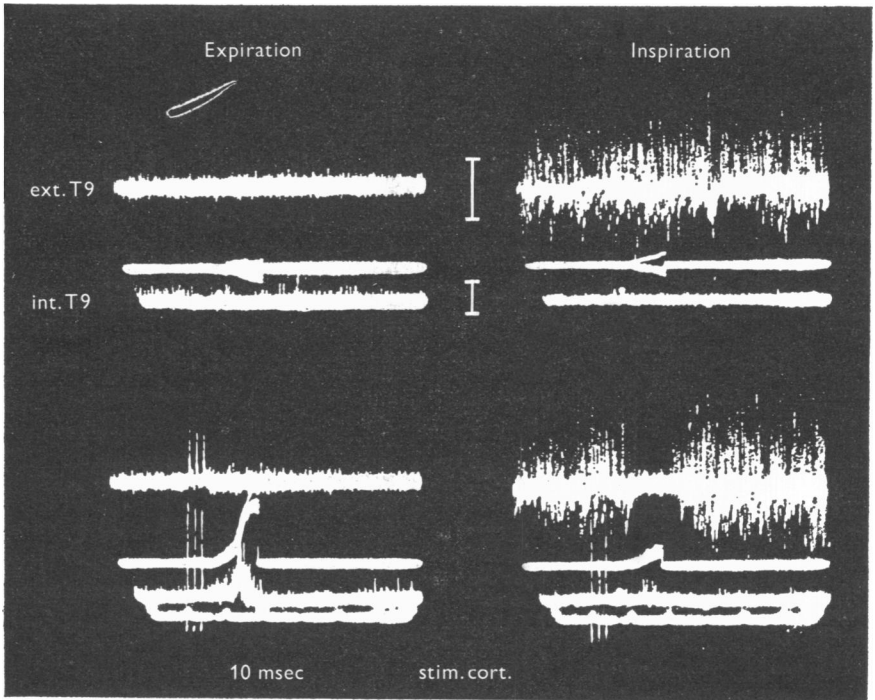


Fig. 6. Interaction between breathing and cortical inputs. In each set of traces, the upper trace is recorded from the external and the lower from the internal intercostal nerves (T9); five superimposed traces, repeated at 6/sec. Middle trace, integral of response in internal intercostal nerve (T9). Calibration $100 \mu\text{V}$. Time marker 10 msec. Upper two sets of traces, control records in expiration and inspiration; lower sets, with cortical stimulation (three shocks, 500 Hz).

In the upper two sets of control records in Fig. 6, the superimposed sweeps show reciprocal activity of inspiratory (ext. T9) and expiratory (int. T9) motoneurons during the inspiratory and expiratory phases of spontaneous breathing. In the lower two sets of records, a brief tetanus to the contralateral sensorimotor cortex evoked a large direct response of expiratory motoneurons during expiration. Conversely, the inspiratory motoneurons showed no reflex response during expiration, but during inspiration their spontaneous activity was inhibited for a period of 15–20

msec. The duration of the inhibition was again longer than that of the direct discharge and corresponded closely with the period of facilitated reflex transmission to expiratory motoneurons revealed in the cortical and segmental conditioning curves (Figs. 2 and 4). Both the direct response of expiratory motoneurons and the reciprocal inhibition of inspiratory activity was most marked when the brief tetanus of three shocks (500 Hz) to the cortex was repeated at 5–6 per second, thus giving a period of 150–200 msec between tetani. This period was of the same duration as the time necessary for full recovery from the phase of depressed reflex transmission to expiratory motoneurons following conditioning by a cortical or segmental input (Figs. 2 and 4). This inhibitory phase presumably also prevented a sustained discharge of expiratory motoneurons in response to continuous tetanic stimulation of the cortex. On the other hand, continuous tetanic stimulation of the cortex resulted in an increase in the rate of breathing (cf. Kaada, 1951). In other experiments which are not the direct concern of this paper, we have found that the cortical stimuli used evoke long-lasting negative potentials in thoracic dorsal roots (DRPs) similar to the DRPs evoked at cervical and lumbar levels following stimulation of the fore- and hind-limb areas in the sensorimotor cortex (Andersen, Eccles & Sears, 1964).

Figs. 5–8 are typical of records made under Flaxedil in showing little expiratory activity. The reason for this is unknown. Before being paralysed the animals almost invariably showed evidence of internal intercostal muscle activity, especially medially in the regions exposed by removal of the longissimus spinalis and iliocostalis muscles.

Dissociation of cortical and breathing inputs to respiratory motoneurons

We thought it likely that the direct response to cortical stimulation is mediated by the cortico-spinal or cortico-rubro-spinal tracts because of its short latency and the distribution of the effective cortical sites (cf. Lundberg & Voorhoeve, 1962; Hongo & Jankowska, 1967). Both the principal corticospinal tract and the rubro-spinal tract lie in the dorso-lateral quadrant of the spinal cord. In contrast, the pathways on which breathing is dependent (Allen, 1927; Pitts, 1940) are carried in the ventrolateral quadrants. We therefore attempted to dissociate the cortical and breathing inputs by selective spinal cord lesions, taking advantage of the segmental innervation of the thorax to obtain recordings above and below the lesions.

In Fig. 7*a* and *c*, superimposed records show the spontaneous activity of inspiratory motoneurons monitored in the external intercostal nerves (lower traces) at the 5th and 8th thoracic segments during mid-inspiration.

Transection of the ventro-lateral quadrant of the spinal cord at the rostral border of the 7th thoracic segment abolished the spontaneous respiratory activity below the lesion (Fig. 7*b*, lower trace) without affecting such activity in the more rostral segment (Fig. 7*c*, lower trace). In contrast, the direct response of expiratory motoneurons to cortical stimulation remained intact below the lesion (Fig. 7*b* and *c*, upper traces) and an intercostal test reflex (Fig. 7*d*) was still facilitated by cortical stimulation at

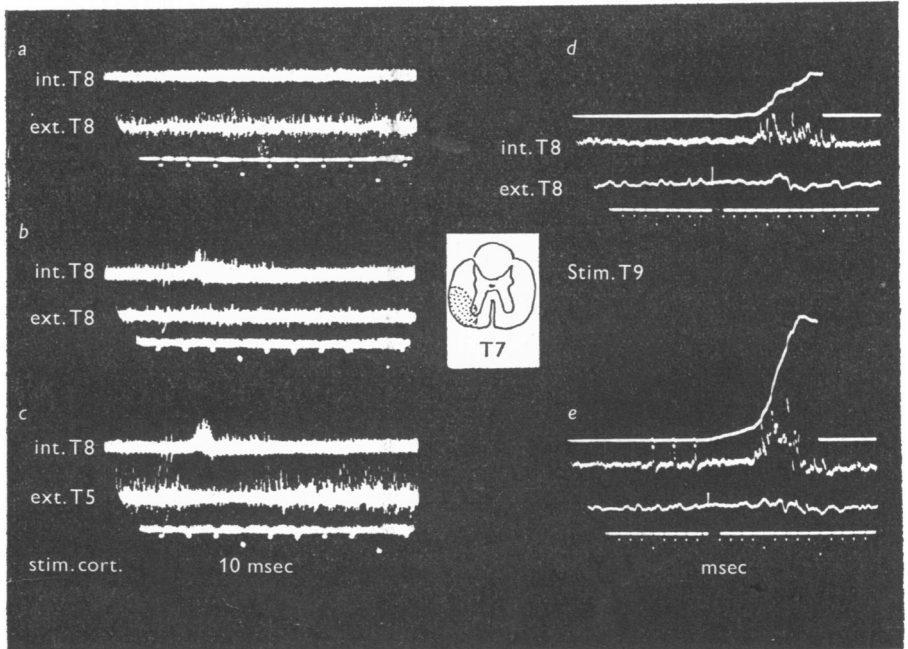


Fig. 7. Dissociation of cortical and breathing inputs by transection of the ventro-lateral quadrant of the spinal cord. In *a* and *b*, upper trace recording from internal and lower trace from external intercostal nerves (T8); 10 msec time marker. In *c*, upper trace as in *a* and *b*, middle trace, recording from external intercostal nerve (T5) above level of transection. Five superimposed traces repeated at 6/sec. *d* and *e*, upper trace integral of response in internal intercostal nerve T8; middle and lower traces recording from internal and external intercostal nerves T8; time marker, 1 msec. *d*, control, *e* cortically conditioned test reflex. Inset, transverse sectional diagram of spinal cord; stippled area represents extent of lesion at T7.

short conditioning intervals (Fig. 7*e*). This dissociation was obtained in three experiments. In a fourth, spontaneous activity which persisted after an ipsilateral ventral quadrant lesion at T5 due presumably to a crossed breathing input (see Pitts, 1946 for references), was subsequently abolished after a contralateral hemisection of the spinal cord at T4.

In Fig. 8 (upper pair), spontaneous inspiratory activity was recorded

from the external intercostal nerve in the 6th thoracic segment (ext T6) and recording made from the internal intercostal nerve at the 9th segment (int. T9). Cortical stimulation (Fig. 8, middle pair) evoked a typical direct response of expiratory motoneurons with reciprocal inhibition of spon-

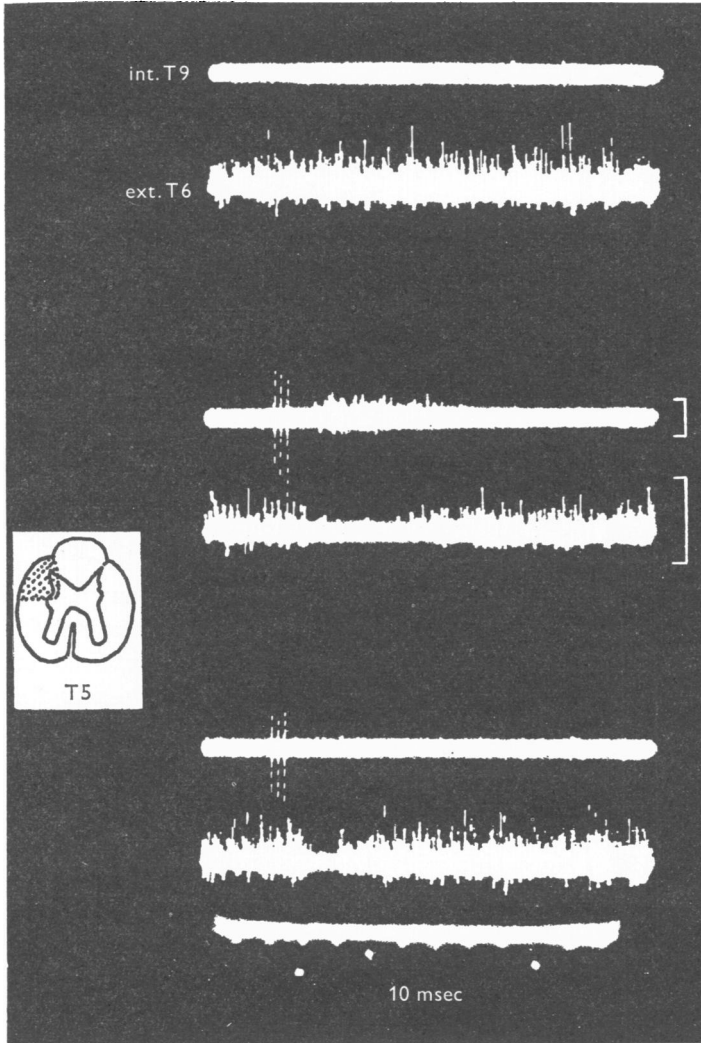


Fig. 8. Dissociation of cortical and breathing inputs by dorsal quadrantic lesion of spinal cord. In each pair of traces, upper recording from internal intercostal nerve, T9, lower from external intercostal nerve T6. Five superimposed traces repeated at 6/sec. Time marker 10 msec. Calibration $100 \mu\text{V}$. Control records in mid-inspiration (upper pair); cortical stimulation (3 shocks, 500 Hz) with recording before (middle pair) and after (lower pair) transection of dorsolateral quadrant of spinal cord (inset diagram).

taneous inspiratory activity. Whereas the spontaneous inspiratory activity persisted after transection of the dorso-lateral quadrant of the spinal cord in the 5th thoracic segment, the direct response of expiratory motoneurons was abolished below the lesion and the duration of the reciprocal inhibition of inspiratory motoneuron activity was considerably reduced (Fig. 8, lower pair). Four similar lesions of the dorsolateral quadrant were made in three other cats and in each case there was a major reduction of the direct responses below the lesion but, as illustrated in Fig. 8, there was never a total loss of the inhibition of spontaneous inspiratory activity, although its duration was always much reduced.

DISCUSSION

The reflex excitation of expiratory motoneurons with reciprocal inhibition of inspiratory motoneurons in the thoracic spinal cord following electrical stimulation of internal intercostal nerves has not been described previously. Its demonstration has depended on the presence of spontaneous (inspiratory) activity in the external intercostal nerves and the use of low intensity stimulation. The failure to demonstrate such reciprocal inhibition in previous investigations (Downman, 1955; Downman & Hussain, 1958; Alderson & Downman, 1966) presumably was due to a low level of inspiratory activity at the segmental levels commonly recorded from (caudal to T8) and to the use of stimuli supra-maximal for reflex activation. The responsible fibres appear to be distinct from those included within the Group 1'b' component of the internal intercostal afferent volley which cause autogenetic inhibition of expiratory motoneurons and from the intercostal Group 1a fibres which like those of the hip adductors (Eccles & Lundberg, 1958) do not cause 'direct' inhibition of their antagonists (Sears, 1964c). Furthermore, they are to be distinguished from the fibres responsible for the intercostal-to-phrenic reflex (Downman, 1955) since this is evoked by muscle but not by cutaneous afferent fibres in the lower intercostal nerves (Decima, Euler & Thoden, 1969) whereas stimulation of cutaneous fibres was effective in the present work. However, in the dog (Sumi & Kotani, 1959), cat (Sumi, 1963a, b) and in man (Kugelberg & Hagbarth, 1959) excitatory and inhibitory reflexogenic skin areas of the trunk have been demonstrated with natural stimulation of the skin (cf. Hagbarth, 1952). It is probable therefore that the reciprocal activation we have described represents a net excitatory effect on expiratory motoneurons exerted reflexly by the cutaneous fibres subserving the reflexes described above, although Groups II and III muscle afferents are possibly also involved. The somatic intercostal-to-intercostal reflexes are mediated by intra-spinal pathways which

disseminate widely throughout the thoracic spinal cord (Downman, 1955) and it is now evident from our observations that these are reciprocally organized with respect to inspiratory and expiratory motoneurons.

A wide variety of responses affecting the rhythm and depth of breathing results from electrical stimulation of the cerebral cortex (Kaada, 1951). We were therefore surprised to find cortical areas from which could be obtained discrete reciprocal activation of thoracic respiratory motoneurons closely resembling the responses to a segmental input. This finding suggests that the cortical responses might be mediated via interneurons of the segmental reflex pathways as proposed for the pyramidal (Lundberg & Voorhoeve, 1962) and rubro-spinal (Hongo, Jankowska & Lundberg, 1969) tracts. The cortical sites stimulated also evoked negative dorsal root potentials (DRPs) in the thoracic roots similar to those evoked in cervical and lumbar dorsal roots by stimulation of the sensorimotor cortex in the fore- and hind-limb areas respectively (Andersen *et al.* 1964). From this we infer that presynaptic inhibition is responsible in part for the long-lasting inhibition of transmission to expiratory motoneurons following a cortical or intercostal conditioning volley. This long-lasting inhibition (as opposed to the earlier short-lasting reciprocal inhibition of inspiratory motoneurons) clearly determines the optimal frequency of repetition (5–6/sec) for obtaining the largest direct response to the cortical or segmental input. These stimulation rates presumably secure the most effective transmission of each input volley to the expiratory motoneurons by avoiding the inhibitory phase occasioned by the conditioning effect of the previous volley (cf. Sumi, 1963*a*). Surface cathodal stimulation was more effective than surface anodal (cf. Livingstone & Phillips, 1957; Hongo & Jankowska, 1967) possibly because repetitive activity was evoked in corticofugal pathways (cf. Hern, Landgren, Phillips & Porter, 1962).

The short latency of the cortical response and its dependence on a spinal pathway traversing the dorso-lateral quadrant implicate either the cortico-spinal or rubro-spinal tracts, both of which are distinct from the principal pathways in the ventral-lateral quadrant subserving the breathing input. The cortically induced inhibition of inspiratory motoneurone activity was never completely abolished by the dorsal quadrant lesions. This residual inhibition could have been due either to a corticofugal inhibition of the cells whose axons convey the excitatory synaptic drive to the inspiratory motoneurons, i.e. be dependent on 'dis-facilitation' or to the excitation of the expiratory driving interneurone (see below) over corticofugal pathways relaying in the brain stem (cf. Rossi & Brodal, 1956; Kuypers, 1958). The precise topography of the cortical areas and tracts responsible for these responses is now being studied and preliminary results seem to

indicate the existence of discrete cortical motor points with centrifugal projections to different segments in the thoracic spinal cord (cf. Figs. 3*a* and *b*).

In Fig. 9 we depict schematically a segmental interneuronal network which could subserve some of the interactions we have described. This simple model is based on the reciprocal distribution of the excitatory and inhibitory synaptic drives (breathing input) responsible for the depolarizing and hyperpolarizing phases of the central respiratory drive potentials

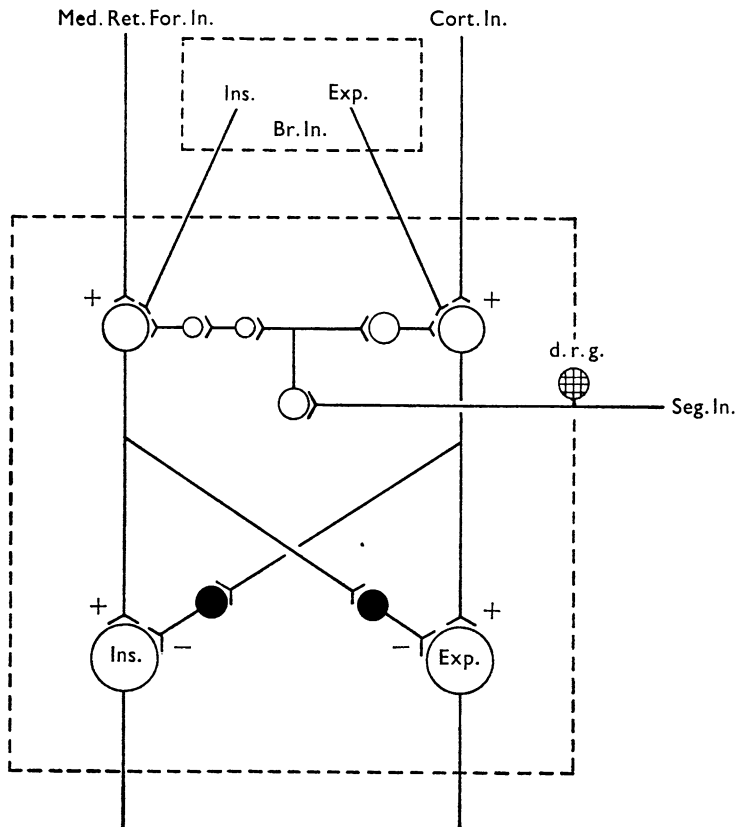


Fig. 9. Schematic representation of interneuronal pathways transmitting reciprocal excitatory and inhibitory actions to respiratory motoneurons. Excitatory interneurons open, and inhibitory filled, circles. Ins., inspiratory motoneurons; Exp., expiratory motoneurons; d.r.g., dorsal root ganglion; Med. Ret. For. In., medial reticular formation input; Cort. In., cortical input; Seg. In., segmental input. Br. In., breathing input (Ins. Inspiratory, Exp. expiratory). Large square (dashed lines) depicts segmental interneuronal network; small rectangle, source of breathing input. A single excitatory interneurone in the diagram may represent a chain of interneurons. See text for operational details.

(CRDPs; Sears, 1964*d*). Inspiratory and expiratory motoneurons are excited through their respective driving interneurons. Concomitant inhibition of the antagonistic motoneurons occurs through inhibitory interneurons which are excited by the driving interneurons.

The expiratory driving interneurone is excited by the segmental input (Seg. In.) the cortical input (Cort. In.) and the breathing input (Br. In.). The weak, longer latency excitatory input to inspiratory motoneurons from the internal intercostal nerve is depicted by the extra interneurone coupling the segmental input with the inspiratory driving interneurone. The inspiratory driving interneurone is excited from the brain stem through the breathing input and through that reticulo-spinal tract which, when stimulated electrically in the medial reticular formation, causes sustained inspiratory apneusis (Pitts, Magoun & Ranson, 1939; Chatfield & Purpura, 1953) with reciprocal inhibition of expiratory activity (Andersen & Sears, 1965, 1970); this latter input is thought not to be concerned directly with rhythmic breathing (Sears, 1966; Andersen & Sears, 1970).

During inspiration, the direct response of expiratory motoneurons to a cortical or segmental input is inhibited, and conversely, these inputs inhibit the spontaneous discharge of inspiratory motoneurons due to the breathing input. During expiration the direct response of the expiratory motoneurons is facilitated while the inhibition of inspiratory motoneurons is concealed due to the absence of spontaneous activity.

This model differs from that subserving the reciprocal innervation of flexor and extensor motoneurons in the rhythmic movements of spinal stepping and scratching, as proposed by Jankowska, Jukes, Lund & Lundberg (1967); their model utilizes reciprocal innervation (mutual inhibition) between interneurons whereas ours, as reasoned above, is based on post-synaptic inhibition.

The monosynaptic excitation of intercostal motoneurons by Group 1 'a' muscle spindle primary afferent fibres (Sears, 1964*c*) clearly bypasses this reciprocal network although the reciprocal activity of inspiratory and expiratory fusimotor neurones in alpha-gamma linkage (Sears, 1963, 1964*b*; Eklund, Euler & Rutkowski, 1964) imposes reciprocal activation on their respective muscle spindles (Critchlow & Euler, 1963). Similarly, anatomical studies have shown that vestibulo-spinal fibres may terminate directly on thoracic motoneurons in the cat (Nyberg-Hansen & Mascitti, 1964), and such monosynaptic connexions by vestibulo-spinal tract fibres on limb fusimotor and alpha motoneurons have been demonstrated physiologically (Lund & Pompeiano, 1968; Grillner, Hongo & Lund, 1969, 1970). Thus it is possible the labyrinthine-cervical reflex control of intercostal motoneurons (Massion, Meulders & Colle, 1960; Corda, Euler & Lennerstrand, 1966) could also bypass the reciprocal network.

We therefore propose as a working hypothesis that the interneuronal network described above is represented at each segmental level of the thoracic spinal cord, where it serves to integrate certain of the different control inputs which converge on spinal respiratory motoneurons.

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