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IMMEDIATE CHANGES IN VENTILATION AND RESPIRATORY PATTERN ASSOCIATED WITH ONSET AND CESSATION OF LOCOMOTION IN THE CAT

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SUMMARY

1. In high decerebrate unanaesthetized cats (pre-collicular/pre-mamillary) which developed spontaneous co-ordinated locomotor activity, ventilation, breathing pattern, phrenic nerve, external and internal intercostal electromyogram (e.m.g.) activities were examined. Locomotion was also induced by electrical stimulation of the subthalamic locomotor region and in a few cases the mesencephalic locomotor region. Quadriceps muscle e.m.g. was used to monitor locomotor activity.

2. Spontaneous locomotor activity was associated with an immediate increase in ventilation and shift of the ventilatory CO_2 response curve to the left. Tidal volume was smaller and respiratory rate larger at any given level of ventilation during spontaneous locomotion. Increases in respiratory rate were due to reductions in both inspiratory and expiratory duration. Upon cessation of locomotion, these changes abruptly returned to control values.

3. Within the first one or two walking steps of spontaneous locomotor activity, the rate of rise of phrenic activity increased slightly while peak phrenic activity remained relatively constant; peak internal intercostal activity increased markedly while peak external intercostal activity decreased.

4. Similar changes in ventilation, phrenic, external and internal intercostal activities were observed in association with locomotion induced by stimulation within the subthalamic or mesencephalic locomotor regions. In contrast to spontaneous locomotor activity, however, increases in both external and internal intercostal activities were often observed.

5. Peak amplitudes of both external and internal intercostal activities increased linearly with increasing levels of end-tidal P_{CO_2} during rest and during locomotion. However, at any given level of P_{CO_2} peak external intercostal activity was smaller and peak internal intercostal activity larger during locomotion than at rest.

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6. With increasing peak quadriceps e.m.g. activity at a constant walking rate, external intercostal activity was progressively inhibited while internal intercostal activity was progressively enhanced. No consistent change in peak phrenic activity was observed with changes in peak quadriceps activity.

7. With increasing walking rate at a constant peak quadriceps e.m.g., peak phrenic and peak internal intercostal activities progressively increased and peak amplitude of external intercostal activity (which was inhibited below the activity observed at rest) also progressively increased.

8. The virtually simultaneous changes in quadriceps activity and respiratory motor activities suggest that the increase in ventilation at exercise onset is neurally mediated. Furthermore, these results suggest that the motor pathways to both the spinal locomotor pattern generators and the pattern-controlling mechanisms for respiration are driven in parallel to provide a quantitative relationship between respiratory motor output and locomotor activity.

9. The functional significance of the alterations in respiratory pattern and participation of the different respiratory muscles is discussed.

INTRODUCTION

It has been well established for almost a century that the onset of exercise in both animals and man is usually associated with abrupt increases in ventilation and cardiac output. The cause of the initial respiratory and circulatory changes has been the subject of a large number of investigations spanning several decades (for reviews see, for example, Bainbridge, 1923; Asmussen, 1965). Predominantly neural mechanisms have been invoked to explain the ventilatory increase because its onset is rapid and results in hypocapnia (Asmussen, 1965; Kao, Mei & Kalia, 1979).

The specific neural pathways and physiological importance of this 'fast component' increase in ventilation still remain uncertain despite extensive research in exercise physiology. Krogh & Lindhard (1913) suggested that 'irradiation' from neural centres involved in the initiation of volitional exercise to respiratory control mechanisms may play an important role. On the other hand, Kao (1963), Kao *et al.* (1979) and F. F. Kao & S. S. Mei (unpublished observations) have demonstrated the participation of neural reflexes from contracting limb muscles in the ventilatory increase of exercise onset.

Animal experimentation addressing these problems has generally employed somewhat artificial methods of inducing or mimicking muscular exercise, for example, by stimulation of ventral roots or motor nerves or by physically squeezing the muscles. The high decerebrate or 'thalamic' cat which spontaneously develops episodes of co-ordinated walking movement (Shik, Severin & Orlovsky, 1966, 1967; Orlovsky, 1969) would seem to offer a more appropriate preparation for the study of the co-ordination of locomotor exercise and respiration. Recent work by Eldrige, Millhorn & Waldrop (1981) and DiMarco, Enler, Romaniuk & Yamamoto (1981) has provided ample confirmation concerning the usefulness of this preparation. A neurally mediated increase in ventilation with exercise was demonstrated by these authors. This preparation, therefore, would seem to offer a convenient model in which to investigate both the immediate and subsequent changes in respiratory activity associated with locomotion.

In the present investigation, we have used this preparation to study in greater detail the rapid non-chemically mediated changes in ventilation at the onset and offset of exercise. Changes in phrenic efferent activity, internal and external intercostal electrical muscle activity and breathing pattern occurring in association with the onset and offset of locomotion were assessed. Locomotor activity was monitored by quadriceps muscle activity.

METHODS

The experiments were performed on twelve adult decerebrate cats weighing between 3·5 and 5·5 kg. A tracheostomy was done following initial anaesthesia with ketamine hydrochloride (Parke-Davis, 10 mg/kg I.M.) and during the remainder of the surgical procedures anaesthesia was maintained by halothane (0·5–1·5 % in air). After cannulation of a carotid artery and jugular vein, the animals were decerebrated at a high brain-stem level anterior to the subthalamic nucleus. The dorsal margin of the section was 0·5–1·5 cm rostral to the superior colliculi and extended ventrally to the optic chiasma. After the decerebration, all anaesthesia was withheld.

In this type of preparation, respiratory rate was higher than that usually observed in lightly anaesthetized cats or in cats decerebrated at a mid-collicular level; tidal volume, however, was not significantly different. Consequently, these animals hyperventilated at rest as shown by the relatively low end-tidal P_{CO_2} values (see below). Blood pressure and heart rate were similar to those observed in other cat preparations.

A C5 phrenic root was dissected free and cut distally. The central stump was de-sheathed and prepared for recording from a dorsal approach. Both vagus nerves were dissected free in the neck and prepared to enable vagotomy through a dorsal approach. Later in the experiment the muscles overlying the dorsal 6th–8th intercostal spaces on one side of the body were removed to allow easy access to the intercostal muscles for recording. External and internal intercostal electromyogram (e.m.g.) activities were recorded from adjacent interspaces. Bipolar wire electrodes were inserted into the quadriceps muscle of either the right or left hind limb to obtain e.m.g. signals of the activities of these muscles.

The animal was suspended in a prone position over a variable speed motor-driven treadmill by means of a stereotaxic head-holder and by vertebral clamps. The height of the treadmill was adjusted so that all four extremities could rest on the treadmill belt while in the extended position, and walking movements during spontaneous episodes of locomotion appeared 'normal'. This method of suspension did not interfere either with the locomotor movements or with chest wall motions or configuration.

The phrenic nerve was reached through a dorsal approach which produced some impairment of muscles of the shoulder girdle and their innervation. The recording condition of the phrenic nerve was stabilized by sewing the electrode to the adjacent paravertebral musculature.

Mass efferent phrenic nerve activity, external and internal intercostal e.m.g. and quadriceps e.m.g. were recorded with bipolar electrodes, amplified, rectified, and further processed by RC networks containing third-order Paynter filters providing signals approximating 'moving averages' of the recorded activity (Evanich, Lopata & Lourenco, 1976).

The flow signal derived from a pneumotachograph (Fleisch no. 00) and a differential pressure transducer was electronically integrated to obtain a tidal volume signal. Tidal CO_2 concentrations were measured with an infra-red CO_2 analyser (Gould Goodhart, Capnograph Mark II) with a sampling rate of 0·1–0·2 l./min and response time of 0·2 sec. In most instances the sampling rate and response time appeared adequate for obtaining approximate 'alveolar' CO_2 concentrations. Body temperature was maintained at $37 \pm 0{\cdot}5$ °C by means of an electric heating pad governed by a rectal thermistor probe.

Bipolar needle electrodes with an inter-electrode distance of 1·0 mm were inserted stereotaxically into the subthalamic locomotor region according to the Horsley–Clarke co-ordinates: A 9; L 2; H −3 (Orlovsky, 1969, cf. also Waller, 1940) or in the mesencephalic locomotor region according to the Horsley–Clarke co-ordinates: P 2; L 4; H +1 (Shik *et al.* 1966, 1967; Orlovsky & Shik, 1976). Rectangular pulses with stimulus intensities ranging from 1·0 to 6·0 V (33–62 Hz) were delivered for 0·6–0·8 msec.

The signals of the moving average of phrenic efferent activity, external and internal intercostal muscle activities and quadriceps muscle activity, tracheal pressure, air flow, tidal volume, tidal CO_2 and blood pressure were monitored continuously and could be recorded in any combination on a rectilinearly writing five-channel chart recorder, and also photographically from a storage oscilloscope.

The experiment was not begun until at least 120 min had elapsed following the decerebration and termination of anaesthesia. Studies were performed both during room air breathing and also at multiple levels of steady-state hypercapnia. Different levels of hypercapnia were produced by having the animals breathe different CO_2 concentrations in oxygen from large, 150 l. bags. Measurements were made only after each new gas mixture was inhaled for at least 5 min.

Studies were also performed following bilateral cervical vagotomy.

RESULTS

General observations

Spontaneous locomotion, observed in ten of the twelve animals, lasted for variable periods of time ranging from 5 sec to 17 min and alternated with variable rest periods lasting 30 sec to 40–50 min, during which no locomotor activity occurred unless provoked by stimulation. The duration of these rest and locomotor periods was not related in any obvious manner. In three experiments, although episodes of spontaneous locomotion ceased after 3–4 hr of recording, locomotion could still be induced by electrical stimulation. Locomotion could be consistently provoked by stimulation of the subthalamic locomotion region, while stimulation of the mesencephalic locomotor region yielded more variable results (cf. Orlovsky, 1969).

In cats which exhibited episodes of spontaneous walking activity, locomotion could often be initiated merely by starting the treadmill. During locomotion, walking speed could be increased or decreased by appropriate adjustments of treadmill speed. Turning off the treadmill usually resulted in cessation of locomotion. During central electrical stimulation, the duration of locomotion could be controlled, since termination of the electrical stimulus usually resulted in the cessation of walking.

Although completely co-ordinated movement of all four extremities was observed in about 50% of the animals during spontaneous locomotion, uncoordinated movement of the forelimbs was frequently observed. These abnormalities, in large part, were probably consequent to the impairment of shoulder muscles and their innervation, as mentioned above. More mild degrees of lack of co-ordination which involved isolated uncoordinated movements at one or more forelimb joints were most frequently observed, however. The hind limb, on the other hand, consistently demonstrated virtually normal co-ordinated walking movements spontaneously or during treadmill-induced locomotion.

Locomotion provoked by electrical stimulation within the subthalamic locomotor region often resulted in an asymmetrical, 'halting' gait, and to obtain a well-co-ordinated symmetrical walking pattern it was then necessary to search for an optimum stimulus site (Marshall & Timms, 1980).

Ventilation and breathing pattern associated with locomotion

The changes in ventilation, blood pressure and end-tidal CO_2 associated with spontaneous co-ordinated walking movement are shown in Fig. 1. With the onset of locomotion as indicated by the records of the quadriceps muscle activity, there was

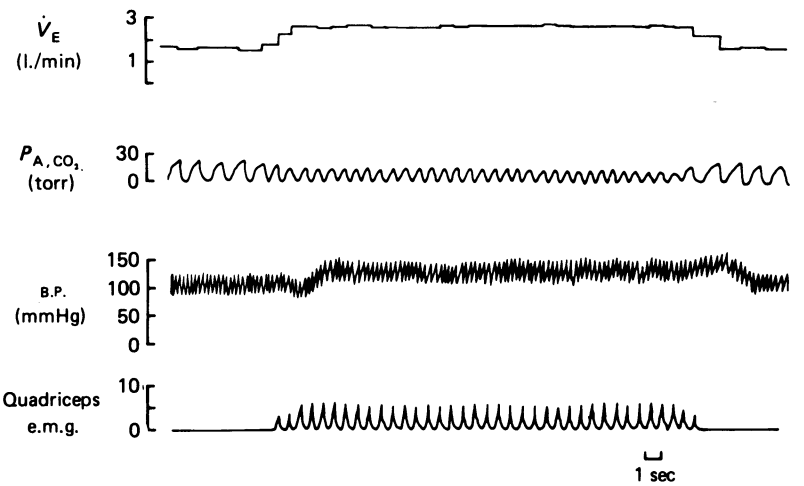

Fig. 1. Changes in ventilation ($\dot{V}_E$), end-tidal P_{CO_2}, and blood pressure (B.P.) associated with the onset and offset of a spontaneous episode of locomotion. Ventilation increases almost simultaneously with the onset of quadriceps e.m.g. activity (relative units).

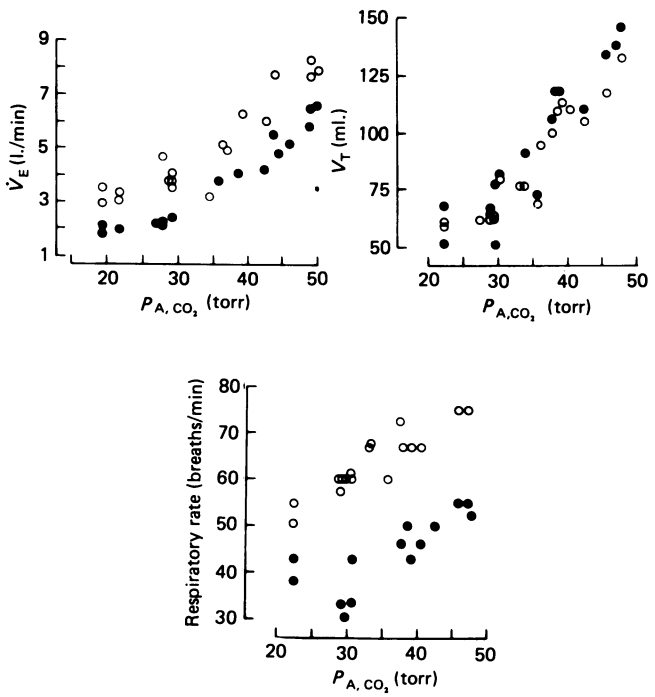

Fig. 2. Ventilatory ($\dot{V}_E$), tidal volume and respiratory frequency responses to hypercapnia while the animal is stationary (●) and during locomotion (○). Compared to the resting state, ventilation and breathing rate are increased during locomotion at any given level of P_{CO_2} while tidal volume is not affected.

an immediate increase in ventilation associated with a small fall in end-tidal P_{CO_2}. A fall in the recorded end-tidal P_{CO_2} values was evident in all instances in which a definite alveolar plateau could be recognized. This was observed in seven of ten animals. In cases where alveolar plateaux were not seen, the fall in P_{CO_2} as shown in Fig. 1 may have been over-estimated. There was also an initial, but brief, decrease in both systolic and diastolic blood pressure followed by a sustained rise in these parameters. This phenomenon was observed in nine of the ten animals. Close examination of the events which occurred at the onset of locomotion revealed that the increase in ventilation frequently began prior to the appearance of quadriceps e.m.g. activity. With the cessation of walking, there was likewise an abrupt fall in ventilation with a return of the end-tidal CO_2 values within a few seconds. Blood pressure also returned to control values. Similar effects were also seen during locomotion induced by starting the treadmill or provoked by electrical stimulation of subthalamic or mesencephalic locomotor regions.

Qualitatively similar effects were also obtained after bilateral vagotomy in five cats. Respiratory rates were somewhat lower and tidal amplitudes higher compared to pre-vagotomy, however. A slight fall in end-tidal P_{CO_2} at the onset of the walking episodes was also seen post-vagotomy.

The interaction between the heightened level of ventilation associated with spontaneous walking and increases in ventilation produced by CO_2-enriched gas mixtures was also evaluated in six cats. Ventilation was measured at multiple levels of steady-state hyperoxic hypercapnia, both at rest (at least 2 min after the preceding walking episode) and during the first two or three walking steps of locomotion. As shown in Fig. 2, a progressive increase in ventilation was associated with increasing end-tidal P_{CO_2} at rest (filled circles). During walking at a constant pace (40 steps/min in this example), there was a higher level of ventilation for any given P_{CO_2} level (open circles). The ventilatory CO_2 response curve showed a parallel shift towards higher ventilation for any given P_{CO_2} value during walking. Ventilations represented at end-tidal P_{CO_2} values of 19–22 torr were obtained with room air breathing. As in this example, all of the experimental preparations hyperventilated significantly also at rest.

Both while at rest and during locomotion, the increase in ventilation in response to increments in end-tidal P_{CO_2} was associated with progressive increases in both tidal volume and respiratory rate provided the vagus nerves were intact; after vagotomy, it was mainly the tidal volume which increased in response to CO_2. At all steady states of end-tidal P_{CO_2}, however, the increase in ventilation associated with locomotion was accomplished predominantly by an increase in breathing rate, the tidal volume response to CO_2 during locomotion being virtually the same as that at rest (Fig. 2*B*, *C*).

The increase in breathing rate in response to locomotion was accomplished by a relative reduction in both inspiratory and expiratory durations (T_I, T_E). The relationship between T_I and T_E present at rest, however, was unchanged during locomotion.

Pattern of respiratory muscle activation associated with locomotion

The changes in efferent motor output to the different respiratory muscles which occurred in association with locomotion were next examined. In Fig. 3*A* repre-

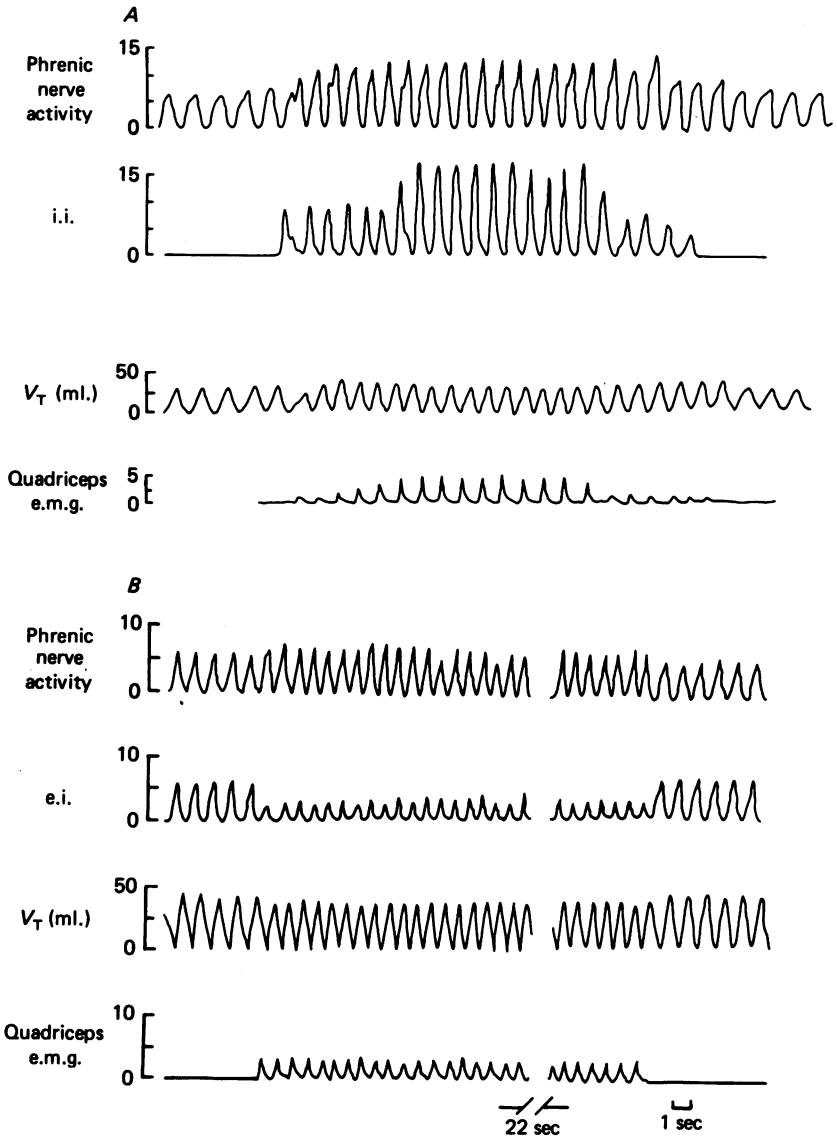

Fig. 3. Changes in phrenic nerve and inspiratory (i.i.) (*A*) and expiratory (e.i.) (*B*) intercostal muscle activities (relative units) associated with spontaneous episodes of locomotion. With the onset of locomotion, inspiratory intercostal muscle activity is inhibited while expiratory intercostal muscle activity is enhanced.

sentative examples of changes in phrenic and expiratory internal intercostal activation in response to the occurrence of spontaneous episodes of walking are shown. The onset of locomotion was associated with an abrupt increase in breathing frequency and peak phrenic activity. Consistently, the onset of walking was associated with the appearance of expiratory e.m.g. activity in the internal intercostal muscles which was absent during resting breathing in nine of ten animals. The opposite effect was seen in the inspiratory external intercostal muscles in which the

e.m.g. activity decreased in every animal during spontaneous locomotor activity as shown in Fig. 3*B*.

The response of peak amplitude of the moving average of the phrenic activity showed some variations; a 10–20 % increase in peak phrenic amplitude occurred in more than 60 % of walking episodes, although instances in which there was no change or even a slight decrease in peak phrenic amplitude were also observed. Such

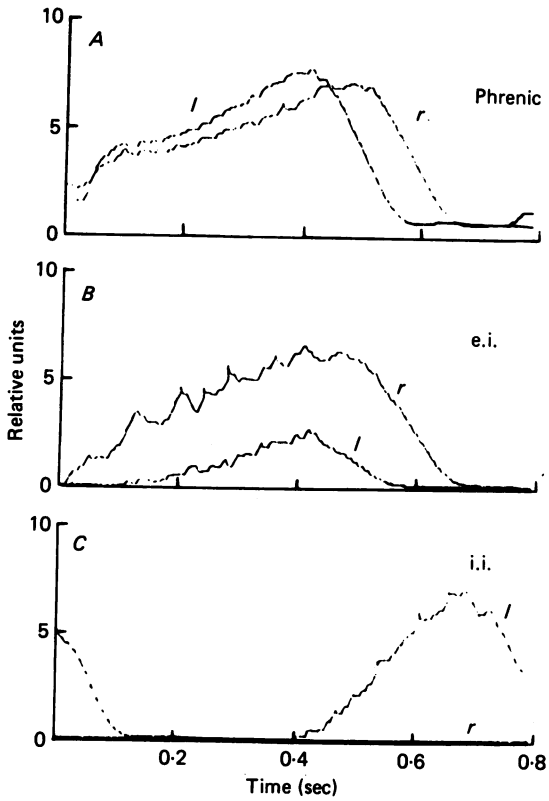

Fig. 4. The computerized averages of five phrenic, external intercostal (e.i.) and internal intercostal (i.i.) trajectories observed during the first one to two walking steps of locomotion (*I*) are superimposed upon the respective computerized average of five trajectories observed while the animal is stationary at rest (*r*). See text for details.

variations in the phrenic response often occurred in the same animal. The factors responsible for these variations could not be discerned. Fig. 4 depicts in greater detail the changes in phrenic, internal and external intercostal activities associated with walking. In this Figure the computerized average of five trajectories observed during the first one to two walking steps of five separate walking episodes is superimposed upon the respective computerized averages of five trajectories observed during resting breathing. Fig. 4*A* shows that walking was associated with a small increase in the rate of rise and a slight increase in peak phrenic activity. Inspiratory external intercostal activity shown in Fig. 4*B* was delayed in onset relative to the onset of phrenic activity and its rate of rise and peak activity decreased during locomotion.

In constrast, the records from expiratory internal intercostal muscles (Fig. 4*C*) showed considerable expiratory activity during walking, whereas such activity was absent at rest.

Fig. 5 illustrates the interaction between these striking effects on internal and external intercostal muscle activity associated with locomotion and the stimulatory effects of increments in P_{CO_2} on the different respiratory motor outputs. The data

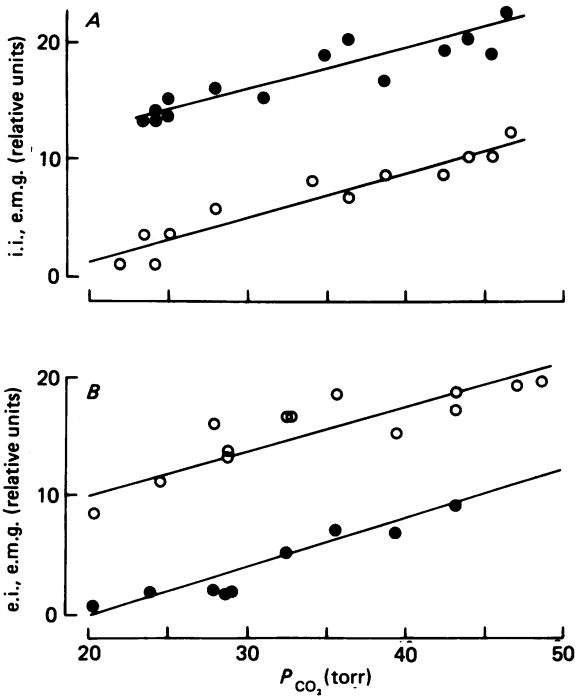

Fig. 5. Peak amplitude of external (*A*) and internal (*B*) intercostal activities at multiple levels of steady-state hypercapnia while the animal is stationary (●) and during locomotion (○). During walking, external intercostal e.m.g. was smaller for any given level of P_{CO_2}. The opposite was true for internal intercostal e.m.g.

points of this Figure were obtained at different levels of steady-state hypercapnia during hyperoxia. This Figure shows that with increasing levels of P_{CO_2}, there was a linear increase in peak amplitude of both external intercostal (Fig. 5*A*) and internal intercostal e.m.g. (Fig. 5*B*). However, at any given level of P_{CO_2}, peak external intercostal activity was smaller and peak internal activity was larger during periods of locomotor activity. The intercostal e.m.g. response curves to hypercapnia during walking were shifted in parallel relative to those obtained during rest periods. This suggested that the inhibition of external intercostal and facilitation of internal intercostal activities were independent of the end-tidal P_{CO_2} level, and that the interaction between CO_2 and locomotor stimuli was mainly of an additive, threshold-changing type. This pattern of motor output to the different respiratory muscles associated with locomotion was similar before and after bilateral vagotomy.

The same general type of changes in respiratory pattern and of motor activity as

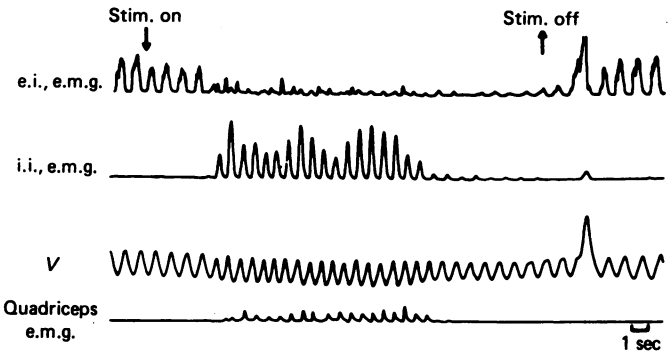

Fig. 6. Changes in external (e.i.) and internal (i.i.) intercostal activities associated with locomotion induced by electrical stimulation (stim.) of a site within the subthalamic locomotor region (A 9; L 2; H-3). Similar responses in intercostal e.m.g.s to those observed during spontaneous locomotion could be produced by electrical stimulation of one of the locomotor areas.

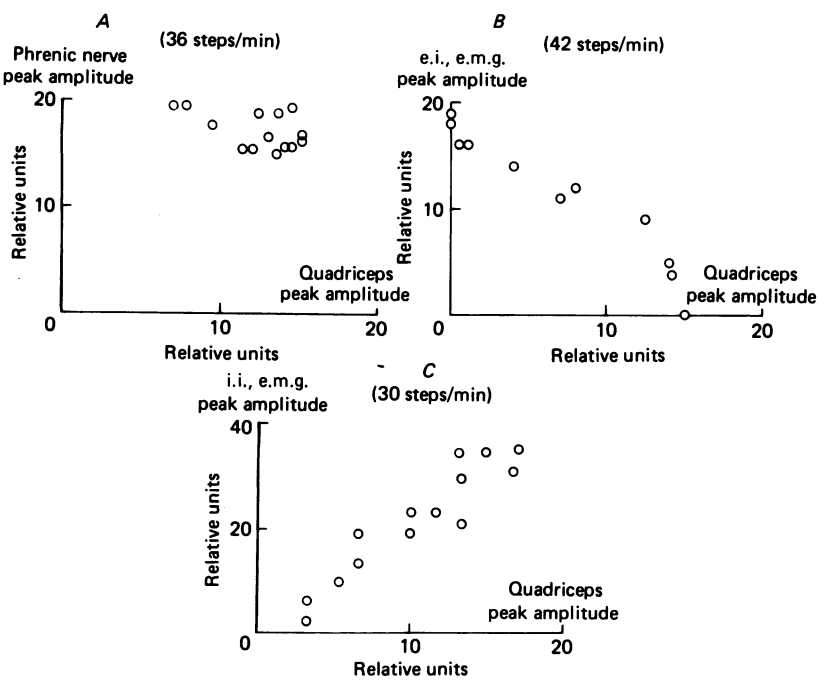

Fig. 7. Changes in peak phrenic nerve activity (*A*) and external (*B*) and internal (*C*) intercostal e.m.g. activities associated with increasing peak quadriceps e.m.g. activity at constant walking rates. See text for further explanation.

those observed during spontaneous episodes of locomotor activity could also be obtained by induction of locomotion by electrical stimulation of the subthalamic locomotor region. A representative response is illustrated in Fig. 6, in which co-ordinated walking movements induced by electrical stimulation were associated with a decrease in the inspiratory external intercostal activity and excitation of

expiratory internal intercostal activity, similar to that observed during spontaneous or treadmill-induced walking. As mentioned earlier, the stimulus site within the subthalamic locomotor region was quite critical for producing well-co-ordinated walking movements. Electrical stimulation of adjacent sites within the subthalamic locomotor region often resulted in different respiratory responses. For example, electrical stimulation of a different site within the subthalamic locomotor region occasionally resulted in excitation of both internal and external intercostal muscles in association with the onset of locomotor activity. Such responses were obtained in the same animal as those of Fig. 6 but were never observed with spontaneous or treadmill-induced locomotion.

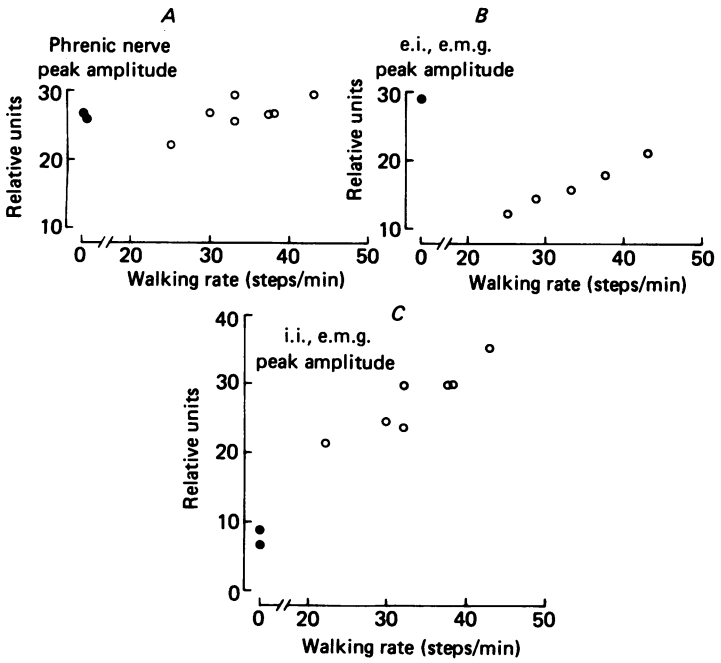

Fig. 8. Changes in peak phrenic nerve activity (*A*) and external (*B*) and internal (*C*) intercostal e.m.g. activities associated with increasing walking rate at a constant quadriceps e.m.g. amplitude. See text for further explanation. (Resting, ●; walking, ○.)

Relationship between respiratory and locomotor outputs

Two indices of locomotor output, namely peak amplitude of 'integrated' quadriceps e.m.g. and walking rate were examined in relation to respiratory motor activities. As illustrated in Fig. 7, at a constant walking rate no consistent relationship was found between the peak amplitudes of phrenic efferent neural and peak quadriceps muscles activities (Fig. 7*A*). But, with increasing peak quadriceps amplitudes external intercostal activity was progressively inhibited (Fig. 7*B*) and internal intercostal activity was progressively enhanced (Fig. 7*C*). The relationships between walking rate and respiratory motor outputs while peak quadriceps e.m.g. remained constant are shown in Fig. 8. With increasing walking rate (steps/min), the

amplitude of peak phrenic neural activity increased slightly (Fig. 8*A*) and the peak amplitudes of external intercostal e.m.g., which were inhibited below the activity observed at rest, also progressively increased with increasing walking rate although never attaining the height of the resting amplitude (Fig. 8*B*). Internal intercostal muscle activity (Fig. 8*C*) also increased progressively and did so relatively much more than the phrenic and external intercostal activities. The respiratory motor outputs thus appeared to be linked to the locomotor activity in a quantitative fashion. Peak intercostal motor outputs seem to be closely linked to locomotor activity and peak phrenic activity to a lesser extent. As shown in Fig. 9, ventilation also progressively increased with increasing walking rate at a constant quadriceps e.m.g. amplitude.

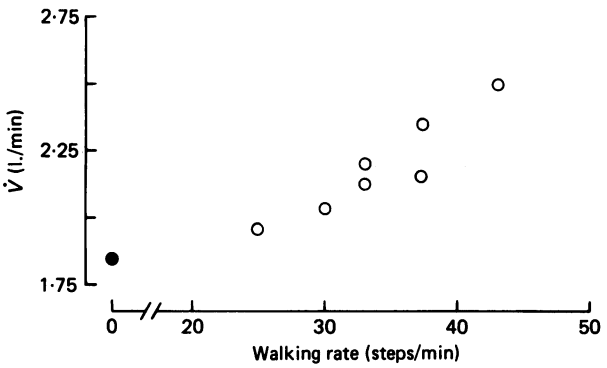

Fig. 9. Changes in ventilation ($\dot{V}$) associated with increasing walking rate. Ventilation increases progressively as walking rate increases. (Resting, ●; walking, ○).

DISCUSSION

The present study confirms the presence in the cat of a neurally mediated increase in ventilation at the onset of exercise. The respiratory changes found in association with the onset of locomotion preceded or occurred simultaneously with the onset of locomotor activity and therefore prior to the influence of any metabolic factors. Likewise, with cessation of locomotion, there was an abrupt return of respiratory activities towards resting values. Furthermore, this time course of changes in respiratory activities was observed during both spontaneously occurring locomotion and locomotion induced by electrical stimulation of the central areas.

Our results support the hypothesis of Krogh & Lindhard (1913), who suggested a neurally mediated increase in ventilation at the onset of exercise in man. They observed abrupt increases in ventilation which occurred virtually simultaneously with the onset of muscular work. Our findings are also in general agreement with the work of Eldridge *et al.* (1981), who studied a similar preparation but with a slightly different technique in that their cats were suspended by a sling around the torso. This method may have placed a significant load on the respiratory muscles causing an alteration in the pattern of respiratory motoneurone output. However, as also shown in the present study, these authors found that the changes in phrenic activity

occurred virtually simultaneously with the onset of locomotion. In agreement with our results, they also reported that co-ordinated locomotor movements and the associated changes in respiratory activity could be elicited by electrical stimulation of the subthalamic locomotor region. This suggests that both respiratory and locomotor output may have a common neural origin.

Eldridge *et al.* (1981) also studied 'fictive' locomotion, i.e. efferent biceps femoris nerve activity induced by electrical stimulation of the subthalamic locomotor area in the completely paralysed animal. Since the described changes in phrenic nerve activity were also present in this preparation, it could be excluded that these effects depend on afferent information from the moving limbs.

In the presence of a hypercapnic ventilatory stimulus, the additional neural stimulus to breathing associated with the induction of locomotion appeared to be roughly equal at all levels of P_{CO_2}. Both the ventilatory and the respiratory e.m.g. response curves to increased P_{CO_2} levels were shifted towards higher response magnitudes for any given P_{CO_2} value, with virtually unchanged slopes during locomotion (cf. Figs. 2 and 5). Stated in other words, the neural stimulus associated with the onset of locomotion appeared to interact with the chemical stimulus in a predominantly 'additive' or 'threshold-changing' manner. This is in agreement with the results of Asmussen & Nielsen (1957) in man.

The qualitative relationship between locomotor output in terms of quadriceps e.m.g. amplitude and walking rate on the one hand, and the various respiratory output parameters on the other, could be demonstrated during either spontaneously occurring locomotion or locomotion induced by central electrical stimulation. These changes in respiratory motor activity observed during locomotion in the unanaesthetized high decerebrate or 'thalamic' preparations could also be produced in light pentobarbitone anaesthetized animals by electrical stimulation of the subthalamic locomotor regions. These results suggest that the motor pathways to both the spinal locomotor pattern generators (see e.g. Grillner, 1981) and the pattern-controlling mechanisms for respiration are driven in parallel to provide a quantitative relationship between the respiratory motor output and the locomotor activity. Whether the fall in P_{CO_2} observed in association with episodes of locomotion is a specific feature of exercise regulation in the cat or merely due to the 'thalamic' preparation remains an open question.

The central neural organization of the corollary inputs to the respiratory controllers from structures involved in locomotor activation may allow ventilation to increase in anticipation of the increase in metabolic requirements. Recent studies of the cardiovascular parameters associated with locomotion (Marshall & Timms, 1980) suggest that cardiac and vasomotor regulation is similarly involved in the co-ordination of reactions elicited at the initiation of locomotor activity, as originally suggested by Johansson (1895). The increased ventilation with exercise was associated with immediate and persistent changes in the pattern of breathing: with the onset of walking movements, ventilation was accomplished by more rapid and shallow breathing when compared to the same level of ventilation at rest. This breathing pattern could possibly function as a mechanism to counteract an anticipated increase in heat production. Alternatively, although we have not encountered any definite correlation between breathing rate and walking rate, we cannot exclude the possibility

that the change in breathing pattern may serve to secure a more optimum function of the muscles about the torso involved in the locomotor movements.

The pattern of activation of the different respiratory muscles varied somewhat during locomotion induced by electrical stimulation of the subthalamic locomotor and mesencephalic regions. The varying respiratory responses to electrical stimulation were not an unexpected finding, since it has been shown previously that the exercise response to stimulation of the locomotor regions is dependent upon the exact stimulus site as well as the intensity of stimulation (Marshall & Timms, 1980). For example, electrical stimulation of one site within the subthalamic locomotor region (cf. Fig. 6) resulted in an immediate inhibition of external intercostal activity. This inhibition began prior to the onset of quadriceps e.m.g. and persisted for several seconds after quadriceps e.m.g. had ceased, suggesting that there may be direct connexions from this stimulus site to the external intercostal neurone pool. Stimulation of adjacent sites within the subthalamic locomotor region, however, occasionally resulted in excitation of inspiratory intercostal activity. The relative contributions of different respiratory muscles to breathing can be modulated therefore in a variety of fashions by activation of structures in the region of the subthalamic locomotor area as well as from the adjacent hypothalamic 'defence area' (A. F. DiMarco, C. von Euler, R. Romaniuk & Y. Yamamoto, in preparation). Since spontaneous or treadmill-induced locomotion can be regarded as being more physiological than electrically induced locomotion and always gave qualitatively identical results, the experimental results of this form of induction of locomotion are emphasized. Most striking was the finding of the dissociation of the effects on phrenic and external intercostal inspiratory activity, with a marked inhibition of the latter in terms of rate of rise, peak amplitude and time of onset. Expiratory internal intercostal activity appeared simultaneously with the onset of locomotion, and the rate of rise and peak activity increased further with increasing locomotor activity despite the shortening of expiratory duration (cf. Figs. 7 and 8).

The inhibition of the inspiratory external intercostal muscle activity associated with the ventilatory increase in response to locomotion contrasts sharply with the response pattern produced by increases in metabolic stimuli such as hypercapnia. The inhibition of external intercostal activity seems to be compensated, at least in part, by the very marked excitation of the expiratory activity of internal intercostal muscles. These differences in response pattern are a further indication that there is a fundamental difference between these two types of ventilatory stimuli. This alteration in the contribution of the respiratory muscles to the work of breathing during locomotion may be functioning to facilitate the induced increase in respiratory rate and to improve the mechanical efficiency of the diaphragm during exercise. The consequent decrease in functional residual capacity (f.r.c.) is in agreement with previous observations in humans that f.r.c. decreases during exercise (e.g. Linnarson, 1974; Yamashiro & Grodins, 1973). The resultant increase in length of the inspiratory muscles may provide them with a mechanical advantage and help preserve the force of contraction and tidal volume despite the increase in respiratory rate during locomotion.

Since qualitatively similar increases in ventilation and changes in the pattern of

activation of the different inspiratory muscles were present after vagotomy, vagal feed-back mechanisms were not significantly influencing the observed responses.

In the present work we have not studied the potential interaction of afferent inputs from exercising limbs and the activation and co-ordination of the respiratory muscles (Kao, 1963; Kao *et al.* 1979; F. F. Kao & S. S. Mei, unpublished observations; Tibes, 1981). The interaction between the central corollary activation of the respiratory controllers and reflex effects from 'ergoreceptive' afferents from the exercising muscles may be important in the fine modulation of both respiratory and locomotor movement.

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