toxin subunits responsible for the clinical manifestations of the syndrome. However, the ability to distinguish staphylococcal isolates should prove of value in examining the epidemiology of TSS and the factors that influence or have influenced the emergence of these strains.

MITCHELL L. COHEN
STANLEY FALKOW*
Departments of Microbiology and Immunology and *Medicine, University of Washington, Seattle 98195*

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Exercise Hyperpnea and Locomotion: Parallel Activation from the Hypothalamus

Abstract. *Unanesthetized decorticate cats walked or ran normally on a treadmill either spontaneously or during electrical stimulation of the subthalamic "locomotor" region. The respiratory response usually preceded the locomotor response and increased in proportion to locomotor activity despite control or ablation of respiratory feedback mechanisms. Respiration increased similarly in paralyzed animals during fictive locomotion despite the absence of muscular contraction or movement. Hypothalamic command signals are thus primarily responsible for the proportional driving of locomotion and respiration during exercise.*

Despite more than a century of study, hypothesis, and debate (*1*), the mechanism leading to hyperpnea, or increased ventilation, during exercise has remained uncertain. The hyperpnea closely parallels the increased metabolic rate resulting from muscular contraction, and therefore arterial CO_2, O_2, and pH remain relatively constant throughout much of the range of moderate exercise. Nevertheless, because of the close relationships between the hyperpnea and metabolic work, many investigators have suggested that chemical receptors variously located in the brainstem (medulla), carotid bodies, lungs, blood vessels, or exercising muscles are the source of stimulation. Others have proposed that neural signals from mechanical receptors in the working muscles or the effects of the exercise-induced increase of body temperature are responsible for hyperpnea. Although such feedback mechanisms exert some influence on respiration under appropriate experimental conditions, no single feedback mechanism, nor any combination of them, has provided a quantitatively adequate explanation for exercise hyperpnea.

An alternative hypothesis is that of a feed-forward mechanism. As long ago as 1913, Krogh and Lindhard (*2*) proposed that neural impulses from the motor cortex that command muscle to exercise also "irradiate" to the respiratory controller in the medulla. Such a mechanism could lead to neurally driven exercise hyperpnea that is proportional to the work performed without the intervention of feedback mechanisms. This hypothesis has never been experimentally validated.

To study the relationship between exercise (locomotion) and respiration in a way in which feedback mechanisms could be eliminated, we used unanesthetized decorticate cats, which Orlovskii (*3*) had shown to walk and run normally on a treadmill. These animals develop locomotion spontaneously as well as during electrical stimulation of the "subthalamic locomotor region" (*3*) and also exhibit "fictive" locomotion in the motor nerves to the legs when the animals are paralyzed with a curare-like agent (*4*).

Our findings support the idea that a neural feed-forward mechanism, originating in the brain at a level above the traditional respiratory centers in the medulla and pons and requiring no feedback mechanisms for its operation, causes both the locomotion and the hyperpnea associated with it.

We decorticated each cat under ether anesthesia, cut the vagus nerves, and denervated the carotid bodies and baroceptors by cutting the carotid sinus nerves. We allowed at least 4 hours for recovery before performing experiments. We measured continuously the carotid arterial pressure, the partial pressure of CO_2 (PCO_2) through a tracheal cannula, and the body temperature, which was kept constant by means of a servo-controlled heater. We quantified respiratory output by measuring the peak integrated electrical activity from the central end of a cut phrenic nerve root (*5*) that was placed in a boatlike bipolar platinum electrode, which we sealed with dental impression material and implanted in the cat's neck. Bipolar electrodes located in both quadriceps muscles allowed quantification of electromyographic (EMG) activity. We then placed the cat's head in a stereotaxic apparatus and suspended the animal over a free-running (not motor-driven) treadmill whose speed could be recorded. A concentric bipolar electrode (*6*) was inserted into the subthalamic locomotor region (*3*) for stimulation (Fig. 1a). At the end of each experiment we perfused the brain in situ with formaldehyde, removed it, and sectioned the diencephalon for histological localization of stimulation sites.

In 9 of 14 experiments, the preparations were successful, and the animals walked spontaneously on the treadmill. An increase in respiration and arterial pressure usually preceded the onset of locomotion, even though there was no increase in end-tidal CO_2 concentration. The cessation of locomotion led to a rapid decrease of both magnitude and frequency of respiration. One animal fortuitously walked spontaneously at two different speeds. The respiratory outputs and treadmill speeds increased proportionately (3229 units per minute at rest, 6735 at a treadmill speed of 14.4 m/min, and 10,815 at 25.9 m/min). Arterial pressure also rose progressively with increasing exercise.

Induction of locomotion by stimulation of the subthalamic locomotor region (*7*) with continuous trains of impulses (30 Hz, 1.0-msec duration) led to similar results. Stimulation caused arterial pressure and respiration to increase promptly, and there was an associated decrease of end-tidal PCO_2 (Fig. 1b). All of these changes preceded the onset of actual locomotion. Ending the stimulation led to cessation of locomotion, a rapid fall in respiration, and a slow decrease in arte-

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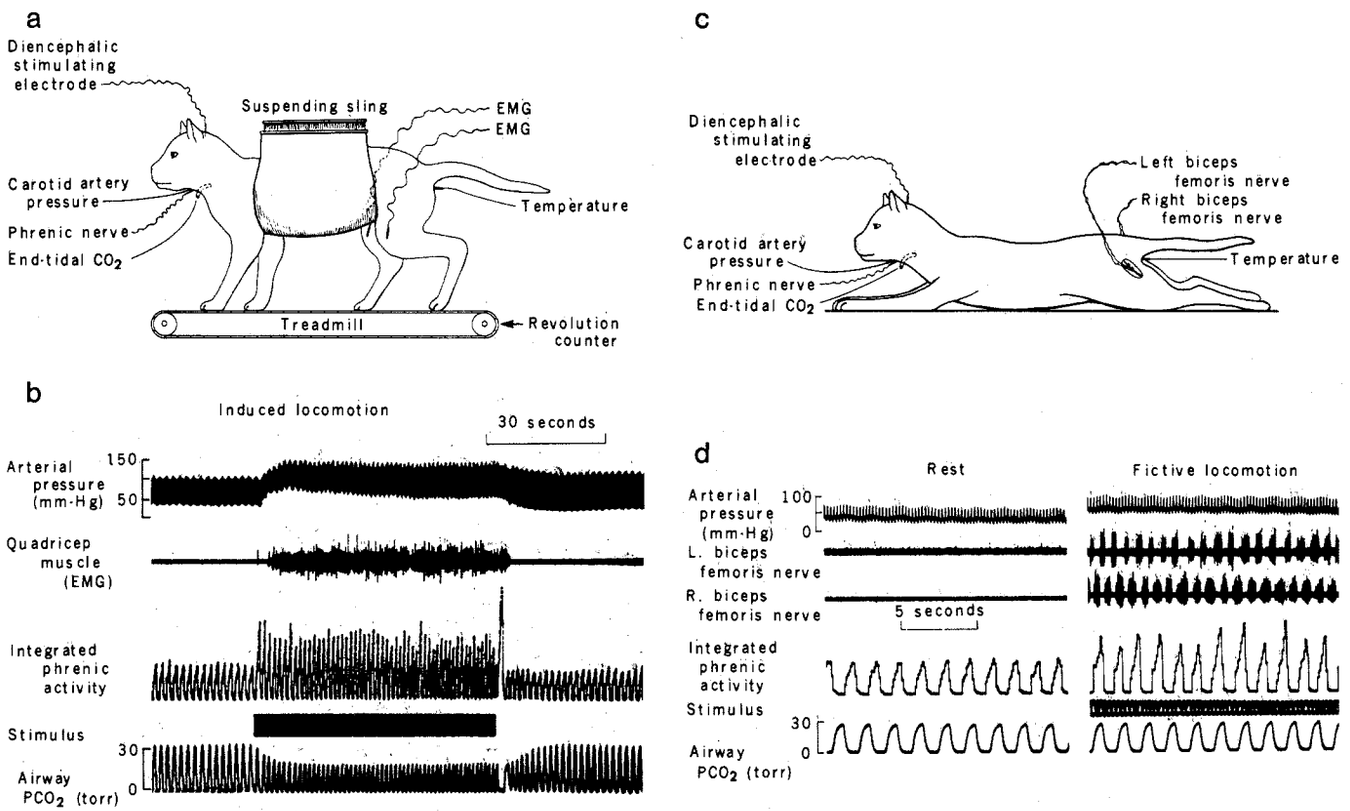

Fig. 1. (a) Decorticate animal preparation used in experiments in which respiratory responses were studied during spontaneous locomotion and locomotion induced by stimulation in the diencephalon. The cat's head was held in a stereotaxic apparatus. Respiratory activity was determined from phrenic nerve recordings. (b) Example of locomotion induced by electrical stimulation of subthalamic locomotor region. (c) Decorticate paralyzed animal preparation used in experiments in which respiratory responses were studied during spontaneous fictive locomotion and locomotion induced by stimulation in the diencephalon. End-tidal PCO_2 was kept constant by means of a servo-controlled ventilator. (d) Example of cardiovascular and respiratory responses during fictive locomotion induced by stimulation of subthalamic locomotor region.

rial pressure toward control values. We examined the relationships between the mean stimulating current at the hypothalamic electrode and the quantitative changes in locomotion and respiration (Fig. 2a). A low mean current caused the respiratory activity to increase from the resting level, but did not produce locomotion. Progressively higher mean stimulating currents led to approximately proportional increases in both respiration and locomotion. Arterial pressure also increased in proportion to the stimulus current.

These studies show that neural signals from the diencephalon can drive locomotion and that respiration increases proportionately without arterial hypercapnia or other feedback from carotid bodies, vagal receptors, or temperature changes. However, because the animals were exercising, we could not absolutely rule out neural feedback from receptors in muscle or moving joints as the cause of the hyperpnea. We therefore studied fictive locomotion in four cats paralyzed with gallamine triethiodide (*8*), prepared as described above except that we recorded electrical activity from both biceps femoris nerves (Fig. 1c) instead of the quadriceps muscles. We maintained end-tidal PCO_2 at a constant level throughout the experiment by means of a servo-controlled ventilator (*9*). Stimulation of the subthalamic locomotor region caused fictive locomotion, shown by motor activity in one or both biceps femoris nerves, and led in all cats to increases of both magnitude and frequency of phrenic bursts and arterial pressure. Figure 1d is an example which has alternating motor activity in the opposing nerves. Figure 2b shows the relationships between hypothalamic mean stimulating current and the changes in respiration and fictive locomotion in this cat. The findings are similar to those for the nonparalyzed animal (Fig. 2a) in that low currents caused

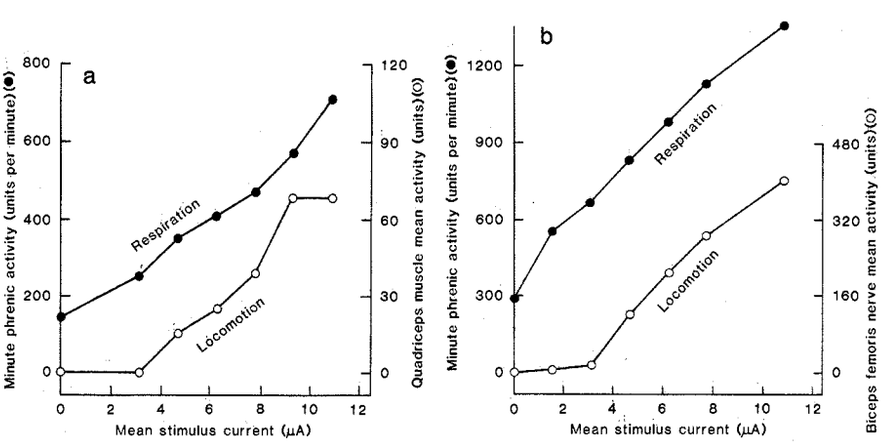

Fig. 2. (a) Responses of respiration (phrenic nerve activity) and locomotion (quadriceps muscle activity) to increasing stimulus current across electrode located in subthalamic locomotor region. (b) Responses of respiration (phrenic nerve activity) and fictive locomotion (biceps femoris nerve activity) to increasing stimulus current across electrode located in subthalamic locomotor region.

respiratory activity to increase without generating locomotion, but progressively higher currents led to proportional increases in respiration and fictive locomotion.

One of the cats spontaneously developed recurring episodes of fictive locomotion, each lasting about 10 seconds. With each episode, respiratory (phrenic) activity and frequency rose in association with the locomotor activity; in most cases the phrenic activity had begun its increase before the onset of biceps femoris nerve activity. Phrenic activity fell promptly when locomotor activity disappeared.

Our experiments demonstrate that automatic locomotion and proportional increases in respiration and arterial pressure, changes that mimic those of natural exercise, can be consistently evoked from a very restricted subthalamic region. The development of similar responses during spontaneous locomotion, which does not occur in the absence of the hypothalamus (*10*), indicates that the evoked responses are due not to fortuitous stimulation of independent pathways but rather to activation of a single hypothalamic mechanism.

Our crucial experiments are those in which both the respiratory and cardiovascular responses occurred during fictive locomotion in the absence of muscular contraction, since they show that actual exercise is not required to produce the responses and thus rule out the causative role of feedback from mechanical receptors in working muscles.

Other workers have reported similar qualitative respiratory or cardiovascular responses during spontaneous locomotion in decorticate cats (*10, 11*) and during electrical stimulation of the hypothalamus in both decorticate animals (*12*) and those with intact brains (*13*). The cardiovascular responses persist after muscular paralysis (*13*) and therefore do not depend on muscular contraction and metabolic changes. Our experiments confirm that the cardiovascular events are independent of muscular contraction.

Our study provides experimental validation of the Krogh and Lindhard feedforward hypothesis (*2*), except that we have shown that the motor cortex is not an essential part of the mechanism. We propose that neural command signals emanating from the hypothalamic locomotor region are primarily responsible for the approximately proportional driving of locomotion and respiration, as well as the cardiovascular adjustments associated with exercise.

Feedback controls are not required for the operation of this mechanism. Nevertheless, the participation of secondary feedback mechanisms during exercise in the intact animal cannot be disregarded. It is likely that they are involved in the fine control of both respiratory magnitude and frequency, and may be responsible for the demonstrated close tracking of ventilation and metabolic events during exercise (*14*).

FREDERIC L. ELDRIDGE
DAVID E. MILLHORN
TONY G. WALDROP

Departments of Medicine and *Physiology, University of North Carolina, Chapel Hill 27514*

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Mutualism Among Sessile Invertebrates: A Mediator of Competition and Predation

Abstract. *Hydroids of the genus* Zanclea *are epizoic on encrusting bryozoans. The bryozoans protect these hydroids with skeletal material.* Zanclea *polyps on the bryozoan* Celleporaria brunnea *sting small predators and adjacent competitors, helping* Celleporaria *to survive and to grow over competing species. This mutualism enables the two species to cover a larger area than they could individually.*

Space is an important limiting resource for many organisms. In marine benthic communities this is most evident for sessile invertebrates and algae inhabiting rocky substrates. For these organisms the habitat exists as discrete patches of limited area. Individuals (or colonies) are restricted to the particular substrate onto which their larvae settle and attach. Population size, survival, and reproductive output are all influenced by the amount of space that is occupied. Competition is often intense and involves the shading, undercutting, or overgrowth of one individual by another (*1–4*). Single species can dominate and sometimes monopolize a patch of substrate. This competitive dominance by one or a few species can be reduced by predators and through the physical disturbance of patches of habitat (*2, 5*).

Competition, predation, and physical disturbance are not the only phenomena that can regulate a species' use of spatial resources. Mutualism, in which two species positively affect one another's abundances, may be equally important (*6, 7*). Mutualistic associations between benthic species have been demonstrated (*3, 7, 8*), but infrequently. In studying the succession of marine invertebrate communities living on experimental panels (*9*), we found an example of mutualism between the bryozoan *Celleporaria* and the hydroid *Zanclea*. The bryozoan protects the hydroid by depositing $CaCO_3$ and the hydroid reduces the impact of competitors and predators on the bryozoan. This association improves the survival of both species and increases the amount of space that they can cover and hold.

Zanclea grow as vinelike colonies in which polyps with capitate tentacles

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