# *Hyperventilation and Spinal Reflexes*

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**The effects of hyperventilation upon dorsal-to-ventral-root spinal reflexes were evaluated in cats to determine whether passive hyperventilation produced during clinical anesthesia affects reflexly-mediated motor activity. The results indicate that both monosynaptic and polysynaptic dorsal-to-ventral-root spinal reflexes are facilitated by hyperventilation, monosynaptic responses more than polysynaptic responses. Monosynaptic responses enhanced by posttetanic potentiation were further facilitated by hyperventilation. Transection of the spinal cord rostral to the site of spinal reflex recording did not abolish the facilitatory effect of hyperventilation upon the spinal reflexes. When the end-expiratory $CO_2$ was kept at control levels (4.0 ± 0.2 per cent) during hyperventilation, reflex facilitation was not seen. It is concluded that hyperventilation facilitates the feline lumbar spinal reflex through the effect of hypocarbia upon the lumbar spinal reflex arc rather than through respiratory reflex activity. The relaxant effects of hyperventilation must be caused by means other than the direct suppression of spinal reflex action as defined by electrical stimulation of dorsal roots. (Key words: Hyperventilation; Spinal reflexes.)**

PASSIVE HYPERVENTILATION during clinical anesthesia allows maintenance of surgical anesthesia with lower concentrations of anesthetic and smaller amounts of muscle relaxants than are required with normal ventilation.[1, 2, 3] The reason for this remains undefined. Changes in function of the neuromuscular junction probably are not responsible, since hypocarbia facilitates neuromuscular transmission.[4] There are, however, indications that hyperventilation significantly alters reflexly mediated motor activity: (1) In anesthetized subjects an active abdominal muscle contraction commonly appears on expiration and can be suppressed by passive overinflation of the lungs on inspiration, suggesting that respiratory stretch reflex activity affects abdominal musculature during anesthesia.[5] (2) Alterations in mean airway pressure affect abdominal and diaphragmatic muscular activity in anesthetized man[6] and in anesthetized cats,[7] suggesting reflexly mediated abdominal muscular responses to stretch of the lungs or the chest wall. (3) Sustained hyperventilation reduces the reflex abdominal muscular response to an electrical stimulus applied to the tails of anesthetized rats.[8] (4) Muscle tension as measured by the integrated electromyogram (IEMG)[9, 10] is decreased by hyperventilation in anesthetized man.[4]

The present study was undertaken to define more closely the effects of hyperventilation on reflex motor activity by measuring dorsal-to-ventral-root spinal reflexes. Suppression of such reflexes should correlate with the decrease of abdominal muscle tension observed clinically. We found, however, that dorsal-to-ventral-root spinal reflexes were, in fact, facilitated by hyperventilation.

## Method

Eight adult cats were studied. Tracheostomy and cannulation of the femoral artery and vein were performed under halothane–nitrous oxide anesthesia. Anesthesia was maintained with 75 per cent nitrous oxide and 25 per cent oxygen plus gallamine triethiodide, administered intravenously by Sage syringe pump at a rate of 70–100 μg/kg/min. Ventilation was controlled by a mechanical respira-

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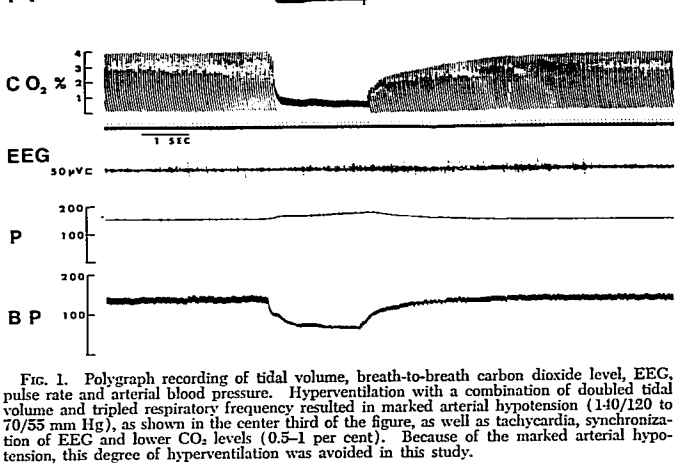


FIG. 1. Polygraph recording of tidal volume, breath-to-breath carbon dioxide level, EEG, pulse rate and arterial blood pressure. Hyperventilation with a combination of doubled tidal volume and tripled respiratory frequency resulted in marked arterial hypotension (140/120 to 70/55 mm Hg), as shown in the center third of the figure, as well as tachycardia, synchronization of EEG and lower $CO_2$ levels (0.5–1 per cent). Because of the marked arterial hypotension, this degree of hyperventilation was avoided in this study.

tor at a tidal volume of 11–14 ml/kg and a frequency of 20–25/min, breath-to-breath end-tidal $CO_2$ maintained at $4.0 \pm 0.2$ per cent. Following laminectomy, the lower lumbar spinal cord was exposed and bathed with mineral oil kept at a constant temperature of 36–37 C via a servo-controlled radiant heat apparatus. Body temperature was maintained at 36–37 C with a servo-controlled circulating warm water blanket. Tidal volume, respiratory frequency, EEG, EKG (lead II), breath-to-breath end-tidal $CO_2$, femoral arterial pressure, rectal temperature, and spinal cord temperature were monitored and recorded continuously. A stimulating Ag–AgCl electrode pair was placed upon the L7 dorsal root, and a recording Ag–AgCl electrode pair upon the L7 ventral root, both roots having been cut distal to the electrode placements. A square-wave pulse of 5v amplitude and 0.1 msec duration provided by a Devices, Ltd. Digitimer was applied to the dorsal root. The response from the ventral root was amplified through a Grass model P511 amplifier, displayed on a Tektronix type 565 oscilloscope, and photographed with a Grass oscilloscope camera, model C4N.

For each measurement, a single stimulus was given every two seconds for a total of five stimuli, and the peaks of the responses were averaged manually.

For posttetanic poteniation, 50 msec of tetanic stimuli at 500 Hertz were given. Single stimuli were then begun two seconds following the onset of the tetanic stimuli, and were repeated every two seconds for a total of five single stimuli. The peak values of the responses thus obtained were averaged manually. To avoid the after-effects of the posttetanic potentiation, five to ten minutes were allowed before the next stimulus was given.

The studies were performed while the lungs were ventilated with 33 per cent nitrous oxide in oxygen, to provide some degree of analgesia, yet exert the least apparent depressant effect upon the reflexes. The effect of inhalation anesthetics on the spinal monosynaptic reflex has been quantitated by de Jong *et al.*[11] who showed that depression of the monosynaptic response is proportional to the logarithm of the inspired anesthetic concentration.[11] In the present experiment, since the concentration of nitrous oxide was kept constant during hyperventilation, and the amplitudes of the

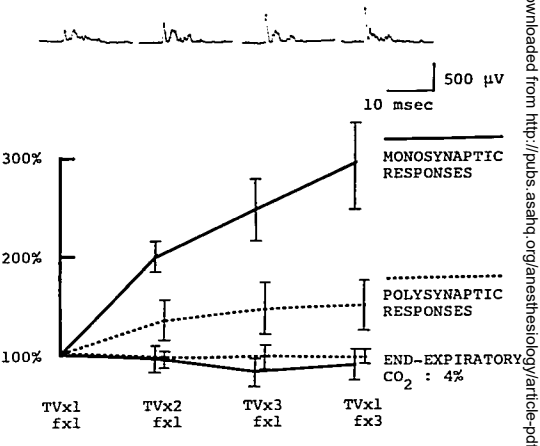


FIG. 2. Changes in reflex response induced by hyperventilation, expressed as per cent of normal (tidal volume × 1, frequency × 1) ventilation (control and mean) value. Top: responses during normal ventilation and hyperventilation, doubled tidal volume (TV × 2), tripled tidal volume (TV × 3), and tripled respiratory frequency (f × 3). The lower two lines represent per cent change in monosynaptic and polysynaptic responses during the same degree of mechanical hyperventilation while end-tidal $CO_2$ was kept at the control level (4.0 ± 0.2 per cent) by addition of $CO_2$ to the inhaled mixture.

reflex spikes were measured after stabilization at different degrees of hyperventilation, it was possible to dissociate the effects of hyperventilation from those of nitrous oxide. Control data were obtained while end-tidal $CO_2$ was kept normal at 4.0 ± 0.2 per cent.[12] The effects of hyperventilation were studied by doubling or tripling the tidal volume, or by tripling the respiratory frequency. The femoral arterial pressure was not altered significantly

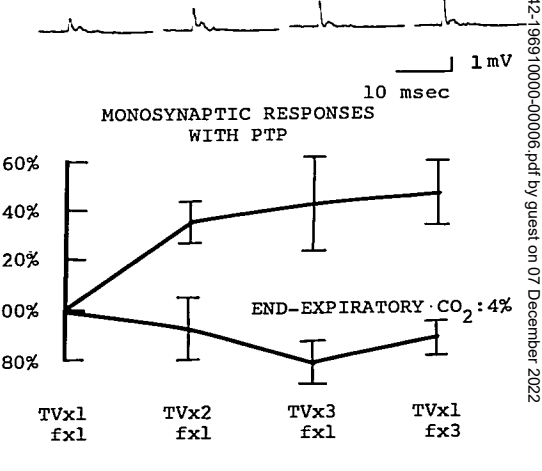


FIG. 3. Changes in monosynaptic responses with posttetanic potentiation (PTP), expressed as per cent of normal ventilation mean control value. Note tenfold lower amplification of the recording compared with that in figure 2, and sixfold increase of control value compared with the response without PTP. The lower line represents per cent change during the same degree of mechanical hyperventilation while end-tidal $CO_2$ was kept at the control level (4.0 ± 0.2 per cent) by addition of $CO_2$ to the inhaled mixture.

TABLE 1. Changes in Response Measures Induced by Hyperventilation, Expressed as Per cent of Normal Ventilation (Mean Control) Value

| | TV ×2 f ×1 (Per cent ± SE) | TV ×3 f ×1 (Per cent ± SE) | TV ×1 f ×3 (Per cent ± SE) |
|---|---|---|---|
| Monosynaptic responses | 199 ± 13* | 246 ± 31* | 291 ± 43* |
| Polysynaptic responses | 137 ± 20* | 146 ± 26* | 149 ± 25* |
| Monosynaptic responses with PTP | 135 ± 18* | 143 ± 19* | 147 ± 13* |
| Monosynaptic responses after spinal cord transection | 197 ± 60*** | 226 ± 56** | 212 ± 68** |
| Polysynaptic responses after spinal cord transection | 120 ± 4* | 121 ± 9** | 132 ± 3* |

* $p < 0.05$. ** $P < 0.10$. *** $P < 0.15$.

by this degree of hyperventilation, but further increases in ventilation, either by rate or by volume, resulted in arterial hypotension (fig. 1).

To evaluate the effects of hyperventilation *per se*, the experiments were repeated in seven animals with 2 to 3 per cent $CO_2$ added to the inhaled mixture to keep end-expiratory $CO_2$ exactly at the control level (4.0 ± 0.2 per cent). To rule out descending effects upon the spinal reflex, the spinal cord in each of four animals was transected at the L2–L3 level, and the experiments were repeated.

## Results

Dorsal root afferent fibers make synaptic connections directly with motoneurons (monosynaptic connections), and synapse on interneurons which, in turn, synapse upon motoneurons (polysynaptic connections). Upon stimulation of the dorsal root, a monosynaptic potential followed by a polysynaptic discharge is recorded in the ventral root (figs. 2 and 3).

Hyperventilation was attained with (1) double tidal volume at control frequency; (2) tripled tidal volume at control frequency; and (3) tripled frequency at control tidal volume. The end-expiratory $CO_2$ levels during hyperventilation were (1) 2.1 to 3.3 per cent (mean 2.8 per cent) at doubled tidal volume; (2) 1.5 to 2.4 per cent (mean 1.9 per cent) at tripled tidal volume; and (3) 1.2 to 1.7 per cent (mean 1.5 per cent) at tripled frequency. All values were accurate to ±0.2 per cent.

During hyperventilation monosynaptic responses showed a significant increase (199 to 291 per cent) in amplitude (fig. 2; table 1). The lower the end-tidal $CO_2$ level, the greater the facilitation of monosynaptic responses. When end-tidal $CO_2$ was kept at control levels (4.0 ± 0.2 per cent) during equal hyperventilation, monosynaptic responses showed no significant alterations.

Polysynaptic response height also showed significant increases (137 to 149 per cent) during hyperventilation, although the magnitude of the increase was not as great as that of the monosynaptic responses (fig. 2; table 1). When end-tidal $CO_2$ was kept at the 4.0 ± 0.2 per cent control level during hyperventilation, there was, again, no significant alteration in height of polysynaptic responses.

Following tetanic stimulation at control levels of ventilation, monosynaptic responses showed approximately sixfold increases in amplitude, compared with responses following a single stimulus (fig. 3). During hyperventilation monosynaptic responses during posttetanic potentiation (PTP) showed a further increase (135 to 147 per cent) which was significant compared with the PTP at control levels of ventilation (fig. 3; table 1). The height of the polysynaptic responses with PTP, however, was not altered significantly by hyperventilation. When the end-tidal $CO_2$ was kept at control levels during hyperventilation, there was, as before, no significant alteration in monosynaptic or in polysynaptic responses during PTP (fig. 3).

Following spinal-cord transection at the L2–L3 level, both monosynaptic and polysynaptic responses showed increases in amplitude during hyperventilation (fig. 4; table 1), with in-

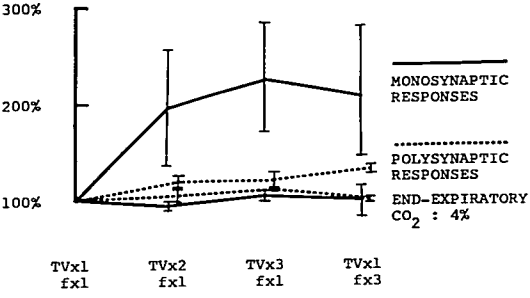


FIG. 4. Changes in response induced by hyperventilation as in figure 2, recordings made after spinal cord transection rostral to the site of the spinal reflex recording (four animals).

creases in monosynaptic responses (197 to 226 per cent) greater than the increases in polysynaptic responses (120 to 132 per cent). When the end-tidal $CO_2$ was kept at control levels during hyperventilation there was again no significant alteration in the height of either monosynaptic or polysynaptic responses.

## Discussion

These results indicate that the spinal reflex following a single stimulus to the feline lumbar dorsal root is facilitated by hyperventilation, in both monosynaptic and polysynaptic responses, the degree of facilitation being greater for monosynaptic responses. The results also indicate that monosynaptic responses are potentiated following tetanic stimulation, and that the potentiated monosynaptic responses following tetanic stimulation are further facilitated by hyperventilation.

When end-expiratory $CO_2$ was kept at control levels during hyperventilation, the same degree of mechanical hyperventilation did not result in the facilitation of the spinal reflex. It seems reasonable to assume, therefore, that the factor responsible for the facilitation of the spinal reflex is the chemical change produced by the lowered $CO_2$ rather than a mechanically mediated effect of hyperventilation.

Since the facilitation of the spinal reflex during hyperventilation was also demonstrated in animals whose spinal cords were transected rostral to the site of the spinal reflex recordings, descending facilitating influences from respiratory muscles or joint receptors on the spinal reflex may be excluded. We may conclude, therefore, that hyperventilation facilitates the feline lumbar spinal reflex because of the effect of hypocarbia upon the spinal reflex arc. These results do not differentiate direct effects of lowered $CO_2$ from those of concomitant increases in *p*H.

These data are in accord with those obtained by Kirstein [13] and by Esplin and Rosenstein,[14] who found that the addition of as much as 40 per cent $CO_2$ to inspired gas mixtures reduced monosynaptic responses when mechanical ventilation was kept constant. The effect of hyperventilation, however, was not studied.

The present results indicate that the effects of hyperventilation upon the spinal reflex are similar to those on the peripheral neuromuscular junction.[15-21] The results do not explain the clinical impression of muscular relaxation associated with hyperventilation, nor do they explain the decreased IEMG activity of the abdominal muscles in man during hyperventilation with general anesthesia. Explanations that may be tenable are that: (1) thoracic and upper lumbar spinal segments are inhibited by hyperventilation, whereas our work was done on the lumbosacral cord region, (2) hypocarbia decreases descending supraspinal facilitation to thoracic and abdominal motoneurons (as might be surmised from the consistent EEG slowing during hyperventilation) (fig. 1), so as to override its predominantly facilitatory effects upon segmental reflexes; or (3) hypocarbia inhibits receptors yet unknown at the periphery. These and similar hypotheses remain to be investigated.

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## Pediatric Anesthesia

**FETAL HYPOGLYCEMIA** Because of the potentially serious nature of neonatal hypoglycemia (convulsions and death), a study of fetal blood glucose levels during maternal labor was made. Fetal hypoglycemia was defined as a blood glucose concentration of less than 40 mg per cent. This occurred in association with four conditions: retardation in fetal growth, pre-eclampsia, accidental hemorrhage, and maternal hypoglycemia. Two of the eight fetuses with hypoglycemia were stillborn. Fetal blood glucose levels were not related to fetal blood $P_{O_2}$ or base excess. Fetal base excess was not altered after injection of 50 g glucose into the mother. The injection of glucagon, one mg, into the fetal scalp increased fetal blood glucose levels to above maternal levels. (*Phillips, L., and others: Fetal Hypoglycemia, Amer. J. Obstet. Gynec. 102: 371 (Oct.) 1968.*)