Transient respiratory augmentation elicited by acute head-down tilt in the anesthetized cat

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Xu, Fadi, Zhong Zhang, and Donald T. Frazier. Transient respiratory augmentation elicited by acute head-down tilt in the anesthetized cat. J. Appl. Physiol. 85(2): 490–496, 1998.—Acute head-down tilt (AHDT, −30°) in humans induces a transient ventilatory augmentation for 1–2 min accompanied by a high venous return. However, the mechanisms underlying this respiratory response remain obscure because of limitations of experiments carried out in human subjects. The present study was undertaken to determine whether AHDT-induced respiratory augmentation exists in the anesthetized, paralyzed, and ventilated cat and, if so, whether this response depends on 1) the cerebellum, 2) the carotid sinus (CS) and/or vagal afferents, and 3) elevation of central venous return. The integrated phrenic neurogram, arterial blood pressure, central venous pressure (CVP), and end-tidal PCO2 were recorded before, during, and after AHDT. The results showed that AHDT produced a transient (−2 min) enhancement of minute phrenic activity (−30%) primarily via an increase in peak integrated phrenic neurogram amplitude associated with a remarkable elevation of CVP (−3 min). Cerebellectomy, CS denervation, bilateral vagotomy, or clamping CVP did not affect the presence of the AHDT-induced minute phrenic activity response. These findings demonstrate that the anesthetized cat is a suitable model for investigating the mechanisms involved in AHDT-induced respiratory augmentation. Preliminary studies suggest that this response does not require the cerebellum, CS/vagal afferents, or an associated rise in central venous return.

Conversely, elevation of respiratory amplitude and/or frequency was elicited by electrical stimulation of given sites within the cerebellar fastigial nucleus (26, 27). Second, the ventilatory response to mechanical stimulation of the gastrocnemius muscle was significantly reduced after ablation of the anterior lobe of the cerebellum (19). In addition, the respiratory response to activation of respiratory muscles of spontaneously breathing cats was also altered by cerebellectomy (4, 30). These results demonstrated that the cerebellum was significantly involved in the respiratory response to alteration of skeletal muscle tone. Third, the cerebellar role in modulation of spinal cord and brain stem mechanisms involved in postural control has been well established (8). The possible contribution of the associated elevation of venous return during AHDT to the respiratory augmentation has been previously considered. Studies have shown that high central venous return can augment respiration by stimulating right ventricular mechanoreceptors via elevation of filling pressure (9, 13) or carotid/pulmonary CO2 chemoreceptors (11, 20, 24, 25) through increasing CO2 flow (product of CO2 concentration and blood flow). It was postulated that the respiratory augmentation during AHDT was the result of increased venous return that subsequently activated chemo- and/or mechanoreceptors [carotid sinus (CS) and vagus nerves]. Direct evidence to support this assumption, however, has not been presented.

The major goal of our study was to determine whether AHDT causes transient respiratory augmentation in the anesthetized cat. If so, potential contributors such as the cerebellum, the carotid or pulmonary chemoreceptors, and an increased central venous return will be investigated. The experiments were conducted in anesthetized, paralyzed, and artificially ventilated cats. Phrenic efferent activity, as an index of respiratory motor drive, was recorded with and without AHDT (−30°) challenge. We found that AHDT produced a transient augmentation in phrenic efferent activity (for ∼2 min) as well as an elevation of central venous pressure (CVP) similar to that observed in humans. We also found that the phrenic responses to AHDT persisted after cerebellectomy, CS denervation, vagotomy, or CVP clamping (maintaining CVP at its control level during AHDT). These results establish that the anesthetized cat is a suitable model to study the mechanisms underlying the AHDT-induced respiratory augmentation. The preliminary experiments presented here were designed to investigate potential contributors, and they reveal that neither the cerebellum nor the high CVP (activation of CS and/or vagal afferents) is essential to the occurrence of this respiratory augmentation.

Acute head-down tilt (AHDT, −30°) has been used to investigate mechanisms underlying the respiratory responses to microgravity or exercise in humans. Relevant studies indicated that AHDT transiently increased minute ventilation within 1–2 min in association with an elevation of venous return (12, 14, 15, 21). Insight into the underlying mechanisms remains somewhat vague, since in human subjects it is difficult to design experiments that separate potential central integrating sites and peripheral afferents responsible for AHDT-induced respiratory augmentation.

Several lines of evidence suggest a possible cerebellar contribution to the AHDT-induced respiratory augmentation. First, recent experiments have demonstrated cerebellar involvement in increased respiratory response to stress. Respiratory responses to hypoxia (29) and hypercapnia (23, 28) were profoundly attenuated after whole or partial ablation of the cerebellum.

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METHODS

Experiments were performed on 13 adult cats (2.5–3.9 kg) of either sex. To limit brain edema resulting from craniotomy and cerebellotomy, dexamethasone (4 mg) was injected 1 day before and on the day of the experiment (2 mg). Anesthesia was initiated in the cat with thiopental sodium (50 mg/kg) and maintained with α-chloralose (40 mg/kg). Supplemental anesthesia was administered as signaled by marked fluctuation in heart rate/arterial pressure and/or presence of eye-blink reflexes. Rectal temperature was monitored continuously (model 73ATA, Yellow Springs Instruments) and maintained at ~38°C via a heating pad and a radiant heat lamp.

General surgeries. The left femoral vein and artery were cannulated. The former was utilized for anesthetic supplement and the latter for monitoring arterial blood pressure (ABP; model P23AA, Statham) and periodic analysis of arterial blood gases (model 1306 pH/blood-gas analyzer, Instrumentation Laboratory). Acidosis, if present, was corrected by addition of bicarbonate (75 mg/ml iv) before the experimental protocols were performed.

Animals were tracheotomized and subsequently paralyzed with gallamine triethiodide (4 mg/kg for induction followed by experimental protocols were performed. Expiratory end-tidal PCO2 and PO2 (PETCO2, PETO2, respectively) were monitored (model 78356A, Hewlett-Packard). The volume and rate of the ventilator were adjusted at an appropriate level for maintaining PETCO2 at ~30 Torr and kept constant in each animal throughout the experiment. The level of PETO2 was maintained at slightly >100 Torr by addition of O2 into the inhaled gas throughout the experiment. After paralysis, supplemental anesthesia was administered as needed whenever abnormal irregularities in elevation of arterial pressure, heart rate, and respiratory rate and pattern were observed.

The cervical segments of both common carotid arteries were isolated via a midline surgical incision and looped with umbilical tape for reduction of hemorrhage by transient occlusion during cerebellotomy. The cervical vagus nerves were carefully isolated and wrapped loosely with a loop of suture for later bilateral transection. Animals were placed prone in a Kopf head and stereotaxic apparatus mounted on a stage. The level of the stage was adjustable to produce whole body AHDT. A dorsal occipital craniotomy was performed, the dura was reflected, and the level of the stage was fixed to determine significance. CS nerves were transectioned (CS denervation). CS vagotomy was subsequently carried out in four cats, and the AHDT was repeated.

RESULTS

Protocol. After baseline cardiorespiratory variables became stable, AHDT was performed by adjusting the head holder to a ~30° position for a fixed time period. Initially, the duration of AHDT was ~5 min. When the transient respiratory augmentation was confirmed to occur ~2 min after the onset of AHDT (see RESULTS), the AHDT duration was shortened to ~2–3 min. To minimize the mechanical fluctuation produced by the sudden change in posture, a period of ~15 s was taken to gradually position the head to the given head-down tilt. The recording electrodes were affixed to the stereotaxic apparatus to maintain a constant contact between the phrenic nerve and the recording electrode during AHDT. AHDT was carried out in six animals, and the same protocol was repeated in five other cats in which the CS nerves were transection (CS denervation). CS nerves were carefully isolated using a ventral approach and confirmed by tracing their origin to the glossopharyngeal nerve. Transection dramatically blunted the respiratory response to inhalation of six breaths of pure N2. AHDT was subsequently repeated when CVP was clamped at its control level by allowing blood volume that shifts, as a result of AHDT, into a syringe attached to the left jugular vein catheter. The blood in the reservoir was slowly (2 min) injected back into the femoral vein after AHDT. Bilateral vagotomy was subsequently performed in three of the five cats, and AHDT was repeated.

During the experiment the raw PN. PN peak), respiratory frequency (f), minute phrenic activity (MPN, product of PN peak, f, and MPN) to AHDT were continuously monitored and recorded on a polygraph (model 7D, Grass) for later data analysis. One hour was generally allowed after completion of each surgical procedure before control values were recorded.

Data analysis. The respiratory variables include the peak value of PN (PN peak), respiratory frequency (f), minute phrenic activity (MPN, product of PN peak, f, and MPN) to AHDT were presented as percent change from control. Baseline (control) cardiorespiratory variables and the changes in MABP, PETCO2, ABP, CVP, and CVP during AHDT were expressed as absolute values. Values are means ± SE. The significant differences of cardiorespiratory responses to AHDT vs. control and among various preparations were examined by utilizing one-way ANOVA with Student-Newman-Keuls test. A one-way repeated-measures ANOVA with post hoc test was used in the protocols where AHDT was repeated after different experimental treatments (e.g., cerebellotomy and vagotomy). P < 0.05 was used to determine significance.
mains (12, 14, 15, 21). They were characterized as a brief (~2 min), significant enhancement of $\int PN_{\text{peak}}$ with little change in $f$. A typical example is shown in Fig. 1, in which the cat was exposed to AHDT for 4 min. Approximately 10 s after initiation of AHDT, CVP displayed a smooth increase (from ~1 cmH$_2$O) and reached a plateau (~6 cmH$_2$O) ~2 min after the onset of AHDT. CVP returned to control values within 1 min after withdrawal of AHDT. A progressive augmentation of $\int PN_{\text{peak}}$ began ~20 s after the onset of AHDT and reached a maximum within 2 min. Thereafter, it started to decline, even though CVP remained at plateau. $\int PN_{\text{peak}}$ gradually returned to its control level ~1 min after the offset of AHDT. MABP showed no pronounced change in response to AHDT. Group data for the respiratory responses in the intact cat are presented in Fig. 2. Compared with control, $\int PN_{\text{peak}}$ and MPN were significantly enhanced to 21.2 ± 6.1 and 28.6 ± 6.0% during AHDT with little change in $f$ (5.5 ± 3.8%). These respiratory alterations ($\int PN_{\text{peak}}$ and MPN) returned to control values within 1 min after termination of AHDT (3.9 ± 3.3 and 4.3 ± 8.7%, P > 0.05).

Cerebellar role in AHDT-induced respiratory response. Cerebellectomy did not significantly alter baseline respiratory variables (Table 1). Similarly, as shown in Fig. 2, the patterns of respiratory responses ($\int PN_{\text{peak}}$, $f$, and MPN) to AHDT were not significantly different from those obtained after removal of the cerebellum. Compared with the intact preparation, the slight decreases in $\int PN_{\text{peak}}$ and MPN after cerebellectomy were not statistically significant. These results suggest that the integrity of the cerebellum is not critical for the AHDT-induced respiratory augmentation.

Effect of CS denervation on AHDT-induced respiratory response. CS denervation did not significantly affect baseline respiratory variables (Table 1). A typical example of respiratory responses to AHDT in a CS-denervated cat is shown in Fig. 3A. The basic characteristics of the respiratory responses to AHDT were similar to those observed in the intact preparation, i.e., a remarkable elevation of $\int PN_{\text{peak}}$ without an apparent change in $f$. Interestingly, group data (Fig. 4) revealed that the amplitude of respiratory augmentation was greater in the CS-denervated than in the intact preparations. The observation that CS denervation increased rather than decreased the respiratory response to AHDT was contrary to our hypothesis and those of other investigators. These data suggest an inhibitory effect of CS nerves on the AHDT-induced respiratory response.

AHDT-induced respiratory response during CVP clamping. An experimental recording that illustrates the effect of CVP on respiratory responses to AHDT is depicted in Fig. 3. Compared with control (Fig. 3A), the respiratory responses were not profoundly altered when the CVP was clamped at its control value during AHDT (Fig. 3B). Group data of the respiratory responses to AHDT with and without the CVP clamped are displayed in Fig. 5. As shown in Fig. 5A, AHDT increased CVP from ~1.5 cmH$_2$O (control) to ~6 cmH$_2$O. When the CVP was clamped during AHDT, its values were very close to the control; however, respiratory excitatory responses ($\int PN_{\text{peak}}$ and MPN) persisted (Fig. 5B). Moreover, none of the respiratory responses to AHDT were markedly different between the preparations with and without CVP clamped.

AHDT-induced respiratory response in vagotomized cats. In seven cats, bilateral vagotomy was carried out after cerebellectomy (n = 4) or CS denervation (n = 3). After bilateral vagotomy, there was an increase in $\int PN_{\text{peak}}$ and a decrease in $f$, leading to an insignificant change in MPN (Table 1). As shown in Fig. 6, the respiratory augmentation in response to AHDT was not eliminated after vagotomy. These findings suggest that AHDT-induced respiratory augmentation is independent of vagal afferents.

Comparison of MABP and PETCO$_2$ response to AHDT in different preparations. Table 2 lists the responses of MABP and PETCO$_2$ to AHDT in the intact, cerebellectomized, CS-denervated, vagotomized, and CVP-clamped preparations. There was a slight tendency to increase MABP and PETCO$_2$ during AHDT in the different experimental preparations tested; however, these changes were not significant.

**DISCUSSION**

AHDT-induced respiratory augmentation in anesthetized cats. One of the major findings in the present study is that AHDT can produce a transient increase in MPN associated with an elevation of CVP in anesthetized cats. This augmented response was a reproducible phenomenon and was elicited ~20 s after the onset of AHDT. It is characterized by a remarkable enhancement of $\int PN_{\text{peak}}$ (~30%) with little change in $f$. These results are consistent with previous studies on humans in whom AHDT caused a transient ventilatory augmentation within 1–2 min (12, 14, 15, 21) via an increase in tidal volume (14, 15) or $f$ (12, 15). The ventilatory response increased 25–38% compared with control (15, 21) with a latency of ~15 s (21). In humans, there was a 200-ml blood volume shift from the peripheral to the
result of simultaneous hyperventilation, since CO2 was PCO2 in humans during AHDT has been explained as a consequence of arterial CO2 pressure (7). The head-down tilt maneuver was conducted from the prone position in the cat, whereas in human subjects the tilt has been generally applied from the supine position (12, 15, 21). However, the similarities of the basic cardiorespiratory responses described above suggest that application of the same degree of AHDT in different positions did not substantially affect cardiorespiratory responses. These comparative findings established the feasibility of utilizing the anesthetized cat model to explore respiratory-related peripheral afferents and central nervous system sites that are critical to the AHDT-induced respiratory augmentation.

As mentioned earlier, some studies on humans infer that ventilatory augmentation during AHDT is due to an elevation of CVP that results in a concomitant increase in CO2 flow. The lack of change in PEtcO2 or alveolar Pco2 in humans during AHDT has been explained as a result of simultaneous hyperventilation, since CO2 was significantly increased (21). To test this assumption, paralyzed cats were used in our experiments. We reasoned that if AHDT produced high CO2 flow through the lungs, as supposed in humans, using the artificially ventilated animal preparation (without hyperventilation) should reveal an increase in PEtcO2 during the period of AHDT. We did observe that PEtcO2 did not increase significantly during AHDT, implying a negligible increase in CO2 flow in the animal preparation. One could argue that the PEtcO2 did not significantly increase during AHDT as a result of the animals' lower metabolism under anesthesia. However, it is clear that the respiratory augmentation to AHDT observed in our experiments cannot be explained by a high CO2 flow passing through the lungs. In awake humans an increase in CO2 flow during AHDT has been postulated. In contrast to the anesthetized and paralyzed cat, this increase in CO2 flow is presumably due to an increased muscle activity induced by posture change.

Phrenic efferent activity was recorded instead of airflow (minute ventilation) so that the AHDT effect on respiratory motor drive could be more directly ascertained. It has been reported that AHDT produces a change of diaphragmatic length (as a result of the shift in the abdominal contents) and tension (16) that could affect ventilation. The fact that phrenic nerve efferent activity was increased in response to AHDT strongly demonstrates that this respiratory augmentation requires central nervous system integration and not just local changes in muscle mechanics. In addition, employing the paralyzed preparation minimized the possible variations of afferent inputs from skeletal muscles activated in the spontaneously breathing cats during AHDT. The inputs, for example, emanating from the diaphragm (4) and limb muscles (7), have been demonstrated to modulate respiration. It would appear that altering muscle afferent activity did not preclude the observed AHDT-induced respiratory augmentation.

Cerebellar involvement. Our observations that cerebellectomy failed to alter AHDT-induced respiratory augmentation suggest that the cerebellum is not essential for this respiratory response. This finding was somewhat surprising, since removal of the cerebellum depresses respiratory augmentation in response to stressed breathing (23, 28, 29), and the cerebellar role in skeletal responses to changes in the muscle tone (posture) is well known (8, 19). We cannot rule out the possibility that the absence of a cerebellar effect during

Table 1. Baseline respiratory variables

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>jPNpeak</th>
<th>f</th>
<th>MPN</th>
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<tr>
<td></td>
<td></td>
<td>(AU)</td>
<td>(Breaths/min)</td>
<td>(AU)</td>
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<tr>
<td>Intact</td>
<td>8</td>
<td>13.9 ± 1.2</td>
<td>23.2 ± 0.9</td>
<td>326.5 ± 33.0</td>
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<tr>
<td>Cerebellctomized</td>
<td>6</td>
<td>15.6 ± 2.1</td>
<td>23.2 ± 0.8</td>
<td>366.3 ± 54.9</td>
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<tr>
<td>CS denervated</td>
<td>5</td>
<td>14.2 ± 1.6</td>
<td>22.4 ± 3.3</td>
<td>337.5 ± 82.0</td>
</tr>
<tr>
<td>Before vagotomy</td>
<td>5</td>
<td>15.2 ± 2.2</td>
<td>23.4 ± 1.0</td>
<td>361.6 ± 59.5</td>
</tr>
<tr>
<td>After vagotomy</td>
<td>6</td>
<td>24.2 ± 2.7</td>
<td>14.6 ± 3.8*</td>
<td>350.5 ± 85.6</td>
</tr>
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</table>

Values are means ± SE; n, number of cats; n = 7 after vagotomy [4 after cerebellectomy and 3 after carotid sinus (CS) denervation]. jPNpeak; peak value of integrated phrenic neurogram; f, respiratory frequency; MPN, minute phrenic activity; AU, arbitrary units; Δ%, changes from intact (vagal intact). *P < 0.05 vs. before vagotomy.

Fig. 2. Comparison of AHDT-induced respiratory augmentation in intact (crosshatched bars, n = 8) and cerebellar cats (filled bars, n = 6). Control levels (0%) for peak value of jPN (jPNpeak), respiratory frequency (f), and minute phrenic activity (MPN) are not shown. Values are means ± SE. *P < 0.05, control (0%, without tilt) vs. tilt.
AHDT is due to the paralyzed preparation, since the alterations in muscle tone induced by AHDT could be profoundly diminished in the paralyzed preparation.

Role of carotid and intrapulmonary chemoreceptors. Another major finding is that the occurrence of AHDT-induced respiratory augmentation is independent of the influence of CS and vagal afferents. These results cast doubt on the hypothesis that AHDT-induced ventilatory augmentation depends on the activation of carotid and intrapulmonary chemoreceptors. Previous studies have indicated that an increase of CO₂ flow passing through the carotid body (11, 20) and lungs (24, 25) produces respiratory augmentation. Therefore, several investigators (12, 21) postulated that AHDT-induced respiratory augmentation resulted from increased CO₂ flow (because of high venous return) that stimulated carotid and intrapulmonary chemoreceptors. Our data strongly argued against this assumption, since AHDT-induced respiratory responses were not eliminated by transection of carotid sinus and vagal nerves innervating carotid and intrapulmonary chemoreceptors, respectively. In contrast, our observation that the respiratory augmentation became greater in the CS-denervated preparation implies an inhibitory effect of the CS nerve on AHDT-induced respiratory augmentation.

The enhancement of respiratory augmentation during AHDT in CS-denervated cats might result from the blockade of carotid baroreceptor afferents. A significant, transient elevation of common carotid arterial pressure was observed in humans within the first 2 min of AHDT (−30°), and this response was not accompanied by significant changes in systemic arterial pressure (14). The latter is in agreement with our results that AHDT in anesthetized cats did not alter MABP significantly. Activation of carotid baroreceptors is reported to inhibit respiration in CS-intact cats but, conversely, increase ventilation in CS-denervated cats (17). In contrast, a decrease in the carotid baroreceptor activity enhances respiration (3). Thus one may logically propose that in CS-intact cats AHDT-induced respiratory responses have been attenuated by increased blood pressure in the common carotid artery because of microgravity induced by AHDT. This assumption is consistent with our finding that AHDT-induced respiratory responses became greater in CS-denervated cats as a result of the absence of the inhibitory effects emanating from the carotid baroreceptors.

The fact that the animals’ PETO₂ was maintained at slightly >100 Torr in the present study suggests that AHDT-induced respiratory augmentation does not depend on activation of O₂ chemoreceptors. In agreement with this finding, Lawler et al. (12) also reported that inhalation of 95% O₂ to blunt activity of the carotid chemoreceptors produced no discernible change in the ventilatory response to AHDT. Carotid denervation...
leads to an attenuation of ventilation when cats are breathing room air (5, 18). However, if an animal was exposed to hyperoxia, ventilation was increased (18). In our study, animals were ventilated with gas mixtures containing high O2 to maintain PETO2 at just 100 Torr. Therefore, it might explain the lack of pronounced changes in baseline respiratory variables observed after CS denervation.

Contribution of mechanoreceptors in right heart. A rise of right ventricular pressure is capable of stimulating mechanoreceptors, subserved by vagal and/or sympathetic afferents (1, 9, 13), that reflexly elevate minute ventilation. A question has been raised as to whether AHDT-produced elevation in CVP stimulates respiration via increased right ventricular pressure. Our observations appear not to support this hypothesis. First, respiratory responses to AHDT did not change markedly when CVP was clamped (Figs. 3 and 5). Second, bilateral vagotomy, which eliminates the major mechanoreceptor inputs from the right heart, failed to alter the respiratory responses to AHDT (Fig. 6). Third, AHDT-induced respiratory augmentation fell toward its control value, even though the CVP response remained at plateau (Fig. 1), demonstrating a dissociation between the respiratory and CVP responses. Although no attempt was made in our study to directly test the effects of sympathetic afferents from the heart, our results appear not to support the notion that the AHDT-induced ventilatory augmentation resulted from stimulation of sympathetic afferents. First, we found that respiratory augmentation persists during AHDT without an increase in CVP. Second, in the present study, no significant increase in ABP was observed. Considering these results, we infer that mechanoreceptors (within the right ventricle) activated by enhancing CVP are not important for eliciting AHDT-induced respiratory augmentation in our experimental preparation.

Other possible factors. Our experiments reported here have clarified that the cerebellum, CS and vagal afferents, and CVP are not required for AHDT-induced respiratory augmentation in anesthetized cats. Although our data cannot conclusively answer where the signals evoked by AHDT are sensed and integrated, our

### Table 2. ABP and PETCO2 responses to AHDT

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<th>MABP, mmHg</th>
<th>PETCO2, Torr</th>
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<tr>
<td></td>
<td>Control</td>
<td>Response</td>
</tr>
<tr>
<td>Intact</td>
<td>140.4 ± 5.4</td>
<td>147.3 ± 5.9</td>
</tr>
<tr>
<td>Cerebellectomized</td>
<td>146.4 ± 8.7</td>
<td>148.5 ± 8.0</td>
</tr>
<tr>
<td>CS denervated</td>
<td>130.5 ± 7.0</td>
<td>142.9 ± 6.5</td>
</tr>
<tr>
<td>Before vagotomy</td>
<td>144.9 ± 9.6</td>
<td>149.1 ± 8.5</td>
</tr>
<tr>
<td>After vagotomy</td>
<td>149.7 ± 8.2</td>
<td>158.9 ± 6.6</td>
</tr>
<tr>
<td>Without CVP clamped</td>
<td>130.5 ± 7.0</td>
<td>142.9 ± 6.5</td>
</tr>
<tr>
<td>With CVP clamped</td>
<td>135.9 ± 7.8</td>
<td>148.4 ± 7.6</td>
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Values are means ± SE; n as in Table 1 footnote. Acute head-down tilt (AHDT)-induced respiratory response was compared with and without central venous pressure (CVP) clamped in 5 cats in which CS nerves had been transected. ABP, arterial blood pressure; MABP, mean ABP; PETCO2, end-tidal PCO2.

![Fig. 5. Comparison of AHDT-induced CVP (A) and respiratory responses (B) with (CVP-C, crosshatched bars) and without CVP clamped (CVP-C, filled bars). Open bars, baseline (before AHDT). Control levels (0%) for PNpeak, f, and MPN are not shown in B. Values are means ± SE. *P < 0.05, control (Ctrl, without tilt) vs. tilt (n = 5).](image-url)
speculation is that AHDT causes an increase in blood flow and CO2 delivery to the brain stem, resulting in enhanced stimulation of central chemoreceptors. In humans, AHDT has been reported to elicit a striking transient elevation of blood flow (27%) (10). Our finding that AHDT-induced respiratory responses persisted in CS-denervated cats does not rule out the possibility that increased CO2 flow within the brain stem excites central chemoreceptors to stimulate respiration. Another possibility would be an involvement of the vestibular system in this respiratory response to AHDT. Anatomically, bulbospinal neurons projecting to phrenic motoneurons have been identified in the medial and lateral vestibular nuclei (2). In decerebrate cats, electrical or chemical (microinjection of glutamate) stimulation of the vestibular nucleus dramatically enhanced the fPNpeak activity (6), indicating that activation of cell bodies residing in the vestibular system has an excitatory effect on respiration. Functional activation of the vestibular system by rotating the head in CS-denervated, vagotomized, and decerebrate cats significantly altered respiration (22). Therefore, the vestibular system may well be involved in the respiratory augmentation during AHDT.

Summary. AHDT-induced cardiorespiratory responses in anesthetized cats are basically similar to those in humans, including 1) a transient respiratory augmentation (−2 min) associated with an elevation in CVP and 2) no significant change in MABP. These findings demonstrate that the anesthetized cat is a suitable model for investigating the mechanisms involved in AHDT-induced respiratory augmentation. Preliminary studies suggest that the respiratory responses to AHDT are not triggered by the integrity of the cerebellum, CS and vagal nerves, and enhancement of CVP.

The authors thank members of the University of Kentucky respiratory group for helpful critiques and Donna Painter and Mandy Frank for assistance in data collection.

This study was supported by National Heart, Lung, and Blood Institute Grant HL-40369.

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Received 12 February 1998; accepted in final form 13 April 1998.

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