

Divergence of Intracranial and Central Venous Pressures in Lightly Anesthetized, Tracheally Intubated Dogs That Move in Response to a Noxious Stimulus

William L. Lanier, M.D.,* Ronald F. Albrecht II, M.D.,† Paul A. Iaizzo, Ph.D.‡

Background: Intracranial pressure (ICP) may increase in tracheally intubated subjects during periods of movement (e.g., "bucking" and coughing). Recent research has suggested that factors other than passive congestion of the cerebral vessels, resulting from increases in central venous pressure, may contribute to the ICP response. The current study evaluated this issue in a canine model of intracranial hypertension and additionally evaluated the relationship between ICP and static increases in superior vena caval pressure.

Methods: Six dogs were lightly anesthetized with 0.65% end-expired halothane in oxygen and nitrogen, and ventilation was mechanically controlled. Intracranial pressure was increased to a stable baseline of 15–20 mmHg using a subarachnoid infusion of warm 0.9% saline solution. The following variables were quantified before, and for 6 min after, initiating a 1-min noxious stimulus to the trachea and skin: ICP, central venous pressure, electromyograms (masseter, deltoid, and intercostal muscles), intrathoracic pressure, and cerebral perfusion pressure (defined as mean arterial pressure – ICP). Later, the protocol was repeated in the presence of neuromuscular block with pancuronium. Finally, in the same dogs, occlusion of the superior vena cava at its junction with the right atrium was used to increase superior vena caval pressure in 5-mmHg increments, from 5 to 30 mmHg, so that the resulting increases in ICP could be quantified.

Results: In unparalyzed dogs whose heads were maintained at the level of the right atrium, there was a 22-mmHg increase

in ICP at 1 min after initiating the noxious stimulus ($P < 0.05$). The ICP increase was related to electromyogram activation and a 6-mmHg increase in central venous pressure; however, it was not associated with significant increases in intrathoracic pressure or cerebral perfusion pressure. Treatment with pancuronium abolished the electromyographic, ICP, and central venous pressure responses to noxious stimulus. When superior vena caval pressure was statically manipulated, the resulting ICP increase was only one half the magnitude of the superior vena caval pressure increase. After elevating the head 14 cm, the ratio of ICP to superior vena caval pressure increases was reduced to one third.

Conclusions: If these results apply to humans, it was concluded that increases in ICP that accompany movement in tracheally intubated patients may arise from two complementary factors: (1) cerebrovascular dilation that correlates with electromyographic activity and is mediated by ascending neural pathways that transmit proprioceptive information, and (2) passive venous congestion that results from any increase in central venous pressure. The influence of the latter factor can be reduced by elevating the head. (Key words: Blood pressure, brain: blood volume; intracranial pressure. Circulation: central venous pressure; mean arterial pressure. Muscle: afferent activity; electromyograms; skeletal. Neuromuscular relaxants: pancuronium.)

TRACHEALLY intubated subjects who move spontaneously or in response to a noxious stimulus (e.g., they cough or "buck on the endotracheal tube") experience increases in intracranial pressure (ICP).¹⁻⁴ The traditional explanation for this phenomenon is that movement results in increases in intrathoracic pressure (ITP), which in turn increases central and cerebral venous blood pressures.^{2,4} Although the traditionally proposed mechanism may account for the ICP increase that occurs in patients who cough actively (and are thus able to close the glottis and increase intrathoracic pressure), it is questionable whether this mechanism completely accounts for the sustained ICP increase observed in tracheally intubated patients.¹ These patients are unable to occlude the airway at the level of the vocal cords. Further, in the case of bucking, the move-

* Professor of Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, Minnesota.

† Resident in Anesthesiology, Mayo Clinic and Mayo Medical School, Rochester, Minnesota.

‡ Assistant Professor of Anesthesiology and Physiology, University of Minnesota, School of Medicine, Minneapolis, Minnesota.

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Address reprint requests to Dr. Lanier: Department of Anesthesiology, Mayo Clinic, Rochester, Minnesota 55905.

ments often lack the sustained, coordinated muscle contractions required to produce meaningful, long-lasting increases in ITP.

Recently, we hypothesized that an additional neural mechanism is important in modulating ICP. Specifically, a stimulated increase in muscle afferent activity (MAA) in response to movement will result in cerebral stimulation accompanied by increased cerebral blood flow (CBF), cerebral blood volume, and ICP.³⁻⁵ The purpose of the current study was to test this hypothesis by observing the ICP, muscle activity, and systemic (ITP, central venous pressure [CVP], arterial blood pressure, and Pa_{CO_2}), responses to a noxious stimulus in unparalyzed and pancuronium-paralyzed, lightly anesthetized dogs. This study was designed to permit the separation of physiologic responses caused by an MAA-mediated mechanism from responses mediated by other sensory receptors (e.g., pain receptors). In addition, to determine the relationship between superior vena caval pressure (SVCP) and ICP, dogs were paralyzed and static increases in SVCP were induced.

Methods

The following protocol was approved by the Institutional Animal Care and Use Committee of Mayo Clinic. Six unmedicated fasting mongrel dogs weighing 16.3 ± 4.3 kg (mean \pm SD) were studied. Anesthesia was induced and maintained during the preparatory period with 1.5–2.5% inspired halothane in oxygen and nitrogen. The trachea was intubated with a 7-mm ID, 29-cm long, cuffed red rubber endotracheal tube, without the use of neuromuscular relaxants. Ventilation was mechanically controlled and adjusted along with FiO_2 to maintain PaO_2 near 150 mmHg and PaCO_2 near 38 mmHg (Instrumentation Laboratory, Lexington, MA; model 1304). Inspired and end-expired oxygen, carbon dioxide, and halothane were measured with a mass spectrometer (Perkin-Elmer, Pomona, CA; model 1100). To prevent air entrainment with coughing during the expiratory phase of the ventilatory cycle, a one-way "J-valve" (Warren E. Collins, Braintree, MA) was placed on the expiratory limb of the Harvard ventilator (Millis, MA). Cannulas were inserted into a femoral artery for blood sampling and mean arterial pressure (MAP) measurements and into a forelimb vein for fluid and drug administration. Heart rate was determined from a lead II electrocardiogram. Electromyograms (EMGs) were recorded from the masseter, deltoid, and intercostal muscles using fine-wire electrodes and a

polygraph (Grass, Quincy, MA; model 78B).⁵ Neuromuscular block was assessed using needle electrodes and a peripheral nerve stimulator (Bard Biomedical, Billerica, MA; Model 750 Digital) to provide supra-maximal stimulation of the hind limb tibial nerve. Degree of block was quantified by visual examination of evoked plantar flexion of the paw. A 33-mm balloon occlusion catheter (Medi-Tech, Watertown, MA) was inserted *via* the right jugular vein until the tip reached the level of the junction of the superior vena cava (SVC) and right atrium. Of the two ports on this catheter, the one near the tip (i.e., the distal port) was used to measure CVP and the second port (i.e., a port that was proximal to the occlusion balloon) was used to measure SVCP. ITP was monitored using an esophageal balloon device.^{5,6} The transducers used to measure CVP, SVCP, and ITP were zeroed at the level of the right atrium. ICP was monitored using a parietal epidural fiberoptic device (LADD Research Industries, Burlington, VT). A PE-50 catheter (Becton Dickinson, Parsippany, NJ) was inserted via a Hustead needle into the lumbar subarachnoid space. Through this catheter, 0.9% saline solution, maintained at 37°C, was infused via an infusion pump at a rate that maintained baseline ICP at a target value of 15–20 mmHg. Body temperature was measured with an esophageal thermistor, and brain temperature was measured with a parietal epidural thermistor (YSI, Yellow Springs, OH; model 73A). The ICP monitoring probe and the epidural thermistor were inserted via small burr holes that were later sealed with cyanoacrylate glue (Borden, Columbus, OH). Both esophageal and epidural temperatures were maintained at $37 \pm 0.5^\circ\text{C}$ (mean \pm range) using heating lamps and pads. During the preparatory period, dogs were given 0.9% saline solution, $20 \text{ ml} \cdot \text{kg}^{-1}$ over 1 h, followed by a maintenance infusion of $5 \text{ ml} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$.

On completion of the above preparation, the dogs were placed in a sling to produce a body position similar to that used in standing (i.e., the vertebral column approximated the horizontal plane and all four paws lightly touched the supporting table).⁵ This was labeled the "neutral position." End-expired halothane concentration was decreased to approximately 0.65% for 20 min. This halothane concentration was intended to provide analgesia and amnesia during the study, yet animals were lightly enough anesthetized so that they would cough and move upon tracheal and skin stimulation.^{5,7} Initially, while the animals were quiescent, control measurements were obtained. Thereafter, a noxious stimulus was delivered to the dogs: The en-

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dotracheal tube was moved back and forth along its longitudinal axis by 2–3 cm for exactly 60 s. The initiation of tracheal stimulation was defined as time = 0 minutes. In addition to tracheal stimulation, dogs simultaneously were administered tetanic-type electrical stimuli of 5 s duration, provided to the upper medial hind limb at 30 and 45 s, using a peripheral nerve stimulator (MiniStim, Professional Instruments, Houston, TX).⁵ After the initiation of stimulation, cerebral and systemic variables were recorded each minute for 6 min.

After the above sequence was complete, the halothane concentration was increased for a minimum of 30 min to allow the animal to again become totally quiescent. Then, the end-expired halothane concentration was again decreased to near 0.65% for 20 min, and the lumbar subarachnoid saline infusion was adjusted, if needed, to provide a baseline ICP value similar to that in the initial control period. Next, the animals were paralyzed with pancuronium 0.2 mg · kg⁻¹. Five minutes later, control variables were measured, and the above study sequence was repeated: i.e. an identical noxious stimulus was used in the unparalyzed and paralyzed portions of the study.

Next, the end-expired halothane concentration was temporarily increased to >0.87% (1.0 MAC), an intercostal space was infiltrated with 0.25% bupivacaine, and a right thoracotomy was performed. The balloon occlusion catheter position was verified and, if needed, adjusted to place the occlusion balloon immediately superior to the azygous vein. The vertical distance between the top of the dog's ear (an approximation of the center of the brain) and the right atrium was recorded. Once again, halothane concentration was decreased to approximately 0.65% end-expired, and ICP baseline was adjusted to 15–20 mmHg. The SVCP transducer was re-zeroed at the level of the right atrium. Baseline ICP and SVCP were recorded. Thereafter, the superior vena cava balloon was inflated to obstruct normal venous drainage until target SVCs of 5, 10, 15, 20, 25, and 30 mmHg were obtained. Once SVCs were stable near the target value, ICP was recorded. The various target pressures were studied in a random sequence. At the completion of this portion of the study, the balloon was completely deflated and, in some dogs, passive baseline pressure again was noted.

Finally, each dog's head was elevated by 14 cm (labeled the "head up position") and saline was infused into the lumbar subarachnoid catheter again to produce a baseline ICP value of 15–20 mmHg. With the SVCP

transducer zeroed to the level of the right atrium, the sequence of measuring ICP in response to SVCP changes was repeated.

At the conclusion of the study, the dogs were killed with intravenous potassium chloride while anesthetized with 1% halothane.

At a given time, the ICP and systemic responses were defined as the mean value obtained over the complete cycle of the mechanical ventilator during periods of quiescence, or the complete cycle of attempted coughing during periods of induced movement. One-way randomized analyses of variance and *post hoc* F-tests were used to compare data after the noxious stimulus to baseline data. Paired t-tests were used to compare data between the paralyzed and unparalyzed portions of the study. The Pearson product-moment correlation coefficient and *t* tests were used to test for associations among the various pressures. All data were expressed as mean ± SD. Values were considered significantly different if they achieved a *P* < 0.05.

Results

Responses to a Noxious Stimulus

Baseline ICP and systemic data were similar in the paralyzed and unparalyzed portions of the study (fig. 1 and table 1). Specifically, baseline ICP was 17 ± 2 mmHg in the unparalyzed state and 17 ± 3 mmHg after paralysis with pancuronium.

The noxious stimulus in paralyzed dogs resulted in no changes in ICP, CVP, ITP, MAP, CPP (defined as mean arterial pressure – ICP), heart rate, or PaCO₂ (fig. 1); and the EMG remained quiescent. In contrast, the noxious stimulus and the resulting movement in unparalyzed dogs produced the expected EMG activation. A summary of the EMG data is presented in table 2. Typically, the dogs coughed and moved vigorously during the first 1 or 2 min after initiating the noxious stimulus; however, activity was diminished thereafter. Although the duration of movement differed from that in our previous study,⁵ the overall quality of the movement was similar. At any instant, movement involved different regions or combinations of regions of the body. There were intermittent diaphragmatic activity (as documented by ITP and CVP fluctuations) and intermittent movements of the forelimb, hind limb, neck, and abdominal and facial muscles.

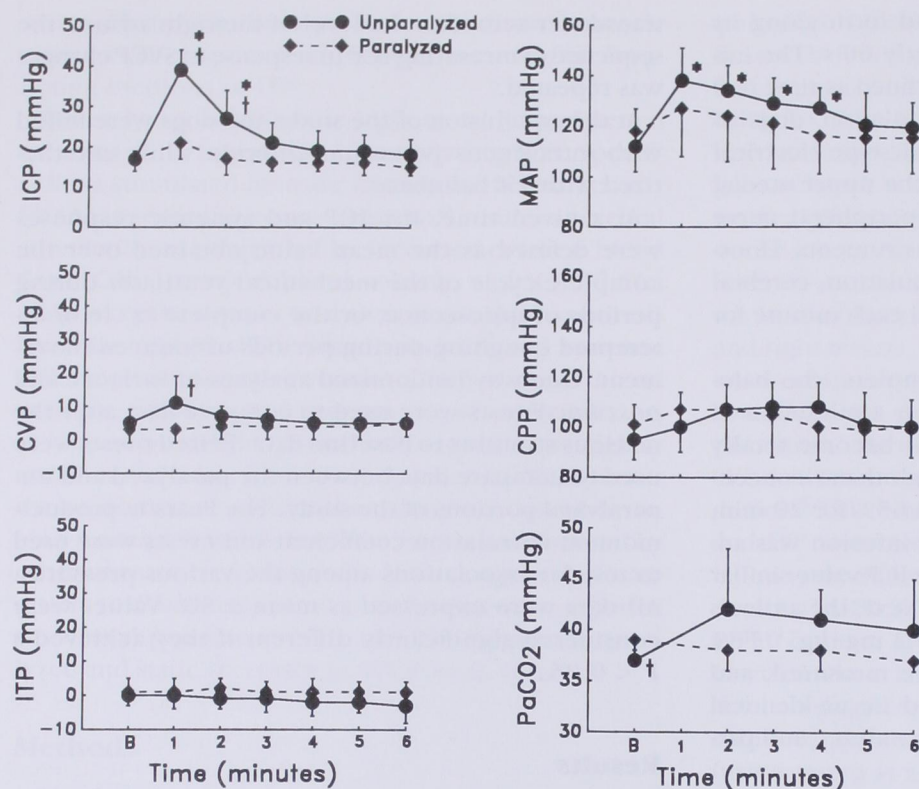


Fig. 1. The effect of a noxious stimulus on intracranial pressure (ICP), central venous pressure (CVP), intrathoracic pressure (ITP), mean arterial blood pressure (MAP), cerebral perfusion pressure (CPP), and PaCO_2 in unparalyzed and paralyzed states. Dogs in an unparalyzed state elicited the greatest amount of movement at the 1- and 2-min time points. Each plotted symbol represents the mean \pm SD. $N = 6$ for all variables except central venous pressure in the unparalyzed portion of the study, where, $N = 5$. B = baseline. * $P < 0.05$ versus baseline values. † $P < 0.05$ versus the unparalyzed state.

During movement, both ITP and CVP transiently varied from baseline. When thoracic movement mimicked coughing activity, exhalatory efforts were typically associated with transient ITP and CVP increases; inspiratory efforts were accompanied by decreases. However, when averaged over the course of the ventilatory or coughing cycle, mean ITP (fig. 1) did not vary from baseline and mean CVP (figs. 1 and 2) changed minimally.

Correlated with the periods of greatest motor activity were increases in ICP (figs. 1 and 2 and table 2). At the 1- and 2-min measurement periods, ICP increases of 22 and 10 mmHg, respectively, were significantly greater than both the baseline values and the corresponding values in the paralyzed state (fig. 1). There were no significant alterations in ITP, heart rate, or PaCO_2 accompanying the ICP increases; however, there was a significant 6-mmHg increase in CVP at the 1-min measurement period. The slight divergence of CVP and ITP at the 1-min measurement period may have resulted from extrathoracic factors (e.g., increased venous return from the limbs and abdomen) influencing the CVP response.

Stimulation in the unparalyzed state resulted in MAP increases at the 1-, 2-, 3-, and 4-min measurement periods that significantly differed from baseline, but not from the response during paralysis. Cerebral perfusion pressure did not change during induced body movement.

When the dogs were unparalyzed, and values from the baseline and poststimulation measurement points were evaluated, there was a significant correlation between ICP and CVP. The regression line was defined by the formula:

$$\text{ICP} = 0.7 \text{ CVP} + 17.4 \quad (N = 35 \text{ data pairs in 5 dogs}; r = 0.37; r^2 = 0.14; P = 0.03)$$

There also were MAP increases that correlated with increases in ICP. The regression line for this relationship was defined by the formula:

$$\text{ICP} = 0.3 \text{ MAP} - 16 \quad (N = 42 \text{ data pairs}; r = 0.51; r^2 = 0.26; P < 0.001).$$

However, there was no apparent association between ICP and CPP ($N = 42$ data pairs; $r = -0.11$; $r^2 = 0.01$; $P = 0.48$).

There also was no association between ICP and PaCO_2 ($N = 24$ data pairs; $r = 0.21$; $r^2 = 0.04$; $P = 0.33$).

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Table 1. Control Cerebral and Systemic Variables Immediately before Administering a Noxious Stimulus

	Treatment Groups	
	Unparalyzed	Pancuronium-paralyzed
PaO ₂ (mmHg)	148 ± 11	156 ± 12
PaCO ₂ (mmHg)	37 ± 1	39 ± 2*
pH	7.35 ± 0.04	7.33 ± 0.04
BB+ (mEq/L)	41 ± 2	41 ± 1
ICP (mmHg)	17 ± 2	17 ± 3
CVP (mmHg)	5 ± 4	3 ± 4
ITP (mmHg)	0 ± 3	1 ± 4
Esophageal temperature (°C)	36.9 ± 0.4	36.7 ± 0.2
Brain temperature (°C)	37.3 ± 0.2	37.1 ± 0.2
MAP (mmHg)	112 ± 15	118 ± 16
Heart rate (beats/min)	96 ± 25	132 ± 30*
Measured halothane (% expired)	0.65 ± 0.05	0.65 ± 0.04

BB+ = buffer base; ICP = intracranial pressure; CVP = central venous pressure; ITP = intrathoracic pressure; MAP = mean arterial blood pressure.

Values are mean ± SD. Six dogs were studied, each of which received two episodes of tracheal and skin stimulation.

* $P < 0.05$.

Intracranial Pressure Response to Static Alteration in Superior Vena Caval Pressure

There was a significant association between static increase in SVCP and ICP. Dogs were initially studied in the neutral position (*i.e.*, the top of the ear was 3 ± 1 cm higher than the right atrium; fig. 3). Baseline ICP was 17 ± 3 mmHg. Under these conditions, the relationship between SVCP and ICP was described by the regression formula:

$ICP = 0.54 \text{ SVCP} + 13$ ($N = 35$ data pairs; $r = 0.85$; $r^2 = 0.72$; $P < 0.001$).

When dogs were placed in the head up position, the ear was 17 ± 1 cm higher than the right atrium, and baseline ICP was adjusted to 17 ± 3 mmHg (fig. 4). Under these conditions, the relationship between SVCP and ICP was described by the regression formula:

$ICP = 0.36 \text{ SVCP} + 12$ ($N = 36$ data pairs; $r = 0.75$; $r^2 = 0.56$; $P < 0.001$).

In three head up and two neutral position dogs, a second baseline ICP was recorded immediately after completing SVCP manipulations. In the former group, the baseline ICP decreased during the study by 3, 5, and 2 mmHg; in the latter group, ICP decreased by 0 and 1 mmHg. There were no meaningful changes in the baseline SVCPs between the two groups. Hence, during the series of studies relating SVCP and ICP, the

baseline elastance characteristics of the intracranial space were not dramatically altered.

Discussion

In this study, movement in response to a noxious stimulus in lightly anesthetized dogs produced a significant increase in ICP that was not related to increases in ITP or CPP. During peak activity, there was a 22-mmHg increase in mean ICP that corresponded with a 6-mmHg increase in mean CVP. It is unlikely that the ICP response to the noxious stimulus and triggered movement were related to activation of pain receptors, because pancuronium, which is neither an analgesic nor anesthetic,^{8,9} abolished the ICP response. Pancuronium, when given to quiescent subjects, has no direct effect on cerebral blood flow, cerebral metabolism, the electroencephalogram, or ICP.¹⁰

In our study, a significant association between ICP increase and EMG activation was observed (fig. 1 and table 2). This association is perhaps best accounted for by the afferentation theory of cerebral arousal.^{3,5,11} Afferentation theory predicts that agents or maneuvers that cause muscle stretch or contraction or directly stimulate muscle stretch receptors (*i.e.*, muscle afferents) will result in cerebral stimulation.^{3,5,11} During active movement, increased MAA correlates with activation of the EMG.^{12,13} The mechanism by which MAA modulates cerebral function was reviewed recently.⁵

In many ways, alterations in cerebral function induced by movement in the current and recent⁵ studies resemble those observed after electrical stimulation of MAA-carrying nerves¹⁴ or intravenous administration of the depolarizing neuromuscular relaxant succinylcholine.^{3,4,11,15-17} Succinylcholine is a potent, and pre-

Table 2. Quantification of Electromyographic Activity after Tracheal Stimulation in Unparalyzed Dogs

Active Channels (n)	Baseline	Time (min)					
		1	2	3	4	5	6
3 of 3		2					
2 of 3		3					
1 of 3		1	4	1	2	2	2
0 of 3	6		2	5	4	4	4

The tabulated numbers represent the number of dogs demonstrating a given number of active electromyographic (EMG) channels. Once the dogs were paralyzed with pancuronium, there was no EMG activity before or after tracheal stimulation.

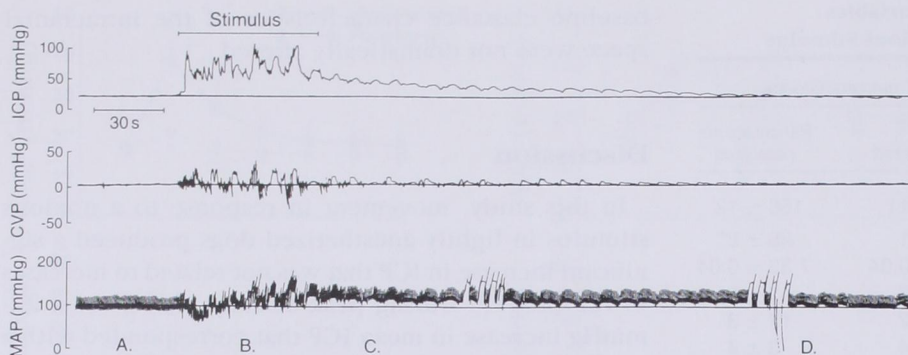


Fig. 2. The relationship among intracranial pressure (ICP), central venous pressure (CVP), and mean arterial blood pressure (MAP) in a lightly anesthetized, mechanically ventilated dog. The horizontal lines approximate the mean baseline values for each variable. Before initiating a noxious stimulus (A), baseline ICP, CVP, and MAP were stable, yet reflected minor fluctuations induced by mechanical ventilation. During delivery of the 1-min noxious stimulus (B), CVP demonstrated positive and negative deflections that correlated with the dog's attempts to inspire and expire. However, the mean

CVP response during this period did not vary meaningfully from baseline. In contrast, mean ICP increased by more than twofold. Early in the stimulus period, MAP decreased at a time when ICP was dramatically increased. Later, MAP increased to—and eventually exceeded—baseline values, such that, cerebral perfusion pressure (defined as MAP-ICP) was not diminished thereafter. After completion of the stimulus (C), the dog continued to move. Mean ICP and MAP values remained elevated at a time in which mean CVP differed little from baseline. As the dog ceased moving (D), both ICP and CVP values returned to baseline. When the same stimulus was initiated after neuromuscular block with pancuronium (data not shown), neither ICP, CVP, nor MAP meaningfully changed from baseline. (Note: the large artifacts in the MAP tracing are the result of sampling blood from—and flushing—the arterial catheter at the 2- and 4-min measurement intervals.)

sumably direct, activator of MAA originating from muscle spindles,^{3,11,15,16} whereas subject movement produces MAA increases owing to a direct, mechanical coupling between extrafusal contractile skeletal muscle and the muscle spindles.^{3,5,12,13,18} Both succinylcholine and movement produce electroencephalographic activation,^{3,5,11,15,16} cerebral blood flow increases,^{3,5,11} and ICP increases.^{1,4,11,17} Pretreatment

with a paralyzing dose of pancuronium, which abolishes MAA increases after succinylcholine or prevented movement after the noxious stimulus used in the current study, also eliminated or attenuates the cerebral response.^{3,5,11,19} By preventing induced movement in the current study, pancuronium may have influenced the activity not only of muscle spindles, but also other populations of proprioceptors (*e.g.*, Golgi tendon organs, cutaneous receptors, and free nerve endings).

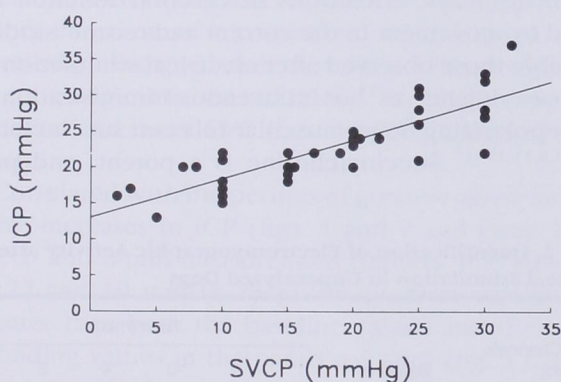


Fig. 3. Correlation between superior vena caval pressure (SVCP) and intracranial pressure (ICP) with the head 3 ± 1 cm above the level of the right atrium (*i.e.*, "neutral position"). There was a significant correlation between superior vena caval pressure and intracranial pressure ($N = 35$ data pairs collected in six dogs; $r = 0.85$; $P < 0.001$), however, the derived regression line (intracranial pressure = 0.54 superior vena caval pressure + 13) had a slope that was less than unity. This implies that only a portion of the superior vena caval pressure increase was transmitted to the head.

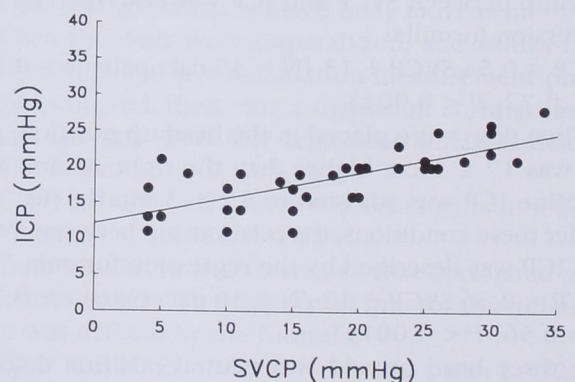


Fig. 4. Correlation between superior vena caval pressure (SVCP) and intracranial pressure (ICP) with the head at a level of 17 ± 1 cm above the right atrium (*i.e.*, "head up position"). There was a significant correlation between the two variables ($N = 36$ data pairs collected in six dogs; $r = 0.75$; $P < 0.001$). However, the derived regression line (intracranial pressure = 0.36 superior vena caval pressure + 12) had a slope that was less than unity. This implies that a very small portion of the superior vena caval pressure increase was transmitted to the head.

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In the current research, regression analysis was used to evaluate the contribution of increases in CVP and SVCP on ICP. In dynamic studies, we discovered that each 1.0-mmHg change in CVP would be expected to change ICP by 0.7 mmHg. This figure was quite consistent with that determined in studies of static alterations in SVCP (*i.e.*, a situation in which there was increased time for equilibration of pressure within the intracranial vault). The latter studies indicated that only one half to one third of the SVCP increase was reflected as an ICP change, depending on whether dogs were in the neutral (fig. 3) or head up (fig. 4) positions. These calculations further suggest that, in our dynamic studies, a mechanism other than passive venous congestion was responsible for the majority of the ICP increase. We assume that the unidentified operant mechanism was mediated by neurally activated cerebral vasodilation.

Our data suggest that there is inefficient pressure transfer from CVP and SVCP to the intracranial vault. This concept is in agreement with previous research in both dogs^{20,21} and humans.²²⁻²⁴ As reviewed by Hibino and Matsuura,²⁰ the venous drainage of the intracranial vault, as it passes toward the heart, contains both collapsible and noncollapsible vessels. Both vessel types—by virtue of their length, diameter, and tortuosity—create a series of resistors that limit pressure transfer.^{18,20} External compression of collapsible vessels also may add to the resistance of the venous system, consistent with a Starling resistor mechanism.^{20,21} Further, in humans, additional resistance may be caused by the presence of a bicuspid valve at the inferiormost portion of the internal jugular vein.²¹⁻²⁴ In its normal functional state, there is a >50% step-down in pressure across the valve during coughing.^{22,24} We are not aware of such valves within the internal jugular vein of the dog; however, the external jugular vein does contain them.²⁴

In interpreting our data, several factors should be taken into consideration: (1) the mechanical aspects of the preparation, (2) the type of movement studied, (3) the duration of movement, (4) the blood pressure response, and (5) baseline cerebral function. Specifically, our study employed dogs that weighed 16.3 ± 4.3 kg and were tracheally intubated with a 7-mm ID tube. The tube was connected to a ventilator equipped with a one-way valve to prevent entrainment of room air during movement. This is a much larger bore tube per unit body mass than would be used in humans. Thus, its use may be expected to attenuate any ITP and

CVP pressure fluxes during movement. Further, when the exhalatory valves of the ventilator were open, the one-way valve would not affect the already attenuated positive ITP and CVP fluxes, but would reinforce any negative pressure fluxes initiated by the dog. Hence, the circuit was biased against numeric increases in ITP and CVP during movement.

In this and our previous study in dogs,⁵ the elicited movement differed from an isolated, classic cough response. Here it was shown that the dogs exhibited some coughing type activity, but it was associated with minimal alterations in mean ITP and CVP. There also was prominent movement in the limbs and other extrathoracic muscle groups. These collective factors were beneficial in separating ITP-, CVP-, and SVCP-dependent processes from the possible neurally mediated influence of activated movements on intracranial physiology. Data from the study supported the hypothesis that increased ascending afferent information generated by *any* muscle activity, and not exclusively the coordinated thoracic muscle activity associated with coughing, contributes to the ICP response. However, one could argue that these same critical study factors may have lessened our ability to extrapolate to the ICP response of tracheally intubated humans whose movement approximates a classic coughing maneuver. In the latter setting, it is possible to produce meaningful increases in ITP.²⁵ Further, our research (figs. 3 and 4) and the research of others,^{20,26-28} suggests that a portion of any ITP pressure changes transmitted to the CVP and SVCP also will be reflected as an increase in ICP.

In our current and previous⁵ studies (fig. 1 and table 2), the cerebral response was highly correlated with the period of movement. In the former,⁵ both movement and the cerebral response (*i.e.*, electroencephalographic activation and a 35% increase in cerebral blood flow) persisted throughout the 6-min study period, and, despite a significant increase in plasma epinephrine concentrations, there was no change in MAP or CPP. In the current study, both movement and the cerebral response ceased before the completion of the 6-min study period. There also was a significant increase in MAP that mirrored the increase in ICP, and thus CPP remained unchanged. Potential reasons for the different durations of movement and blood pressure responses between studies is not clear, but may relate to the only meaningful factor by which the two preparations were known to differ: intracranial elastance. In the former study,⁵ elastance was adjusted so that ICP remained near zero throughout the study; whereas, in the current

study, intracranial hypertension was established. Nevertheless, taken together, these studies suggest that the punctuated coughing response and the MAP response were influenced centrally. The data further suggest that the MAP increase during coughing was not the cause of ICP changes (fig. 2B), but perhaps was a consequence of ICP changes. Of note, the blood pressure response observed in the current study probably is more typical of that observed in humans who move on awakening from anesthesia.²⁹

It should be emphasized that we studied normal dogs that were lightly anesthetized. Consistent with afferentation theory, normal or near-normal baseline cerebral function is critical for the brain to recognize ascending afferent input and mount a response. A severe alteration in baseline cerebral function, whether induced by injury (e.g., resulting from cerebral ischemia)³⁰ or deep anesthesia,¹¹ will attenuate or abolish the cerebral response to increased afferent input. Using succinylcholine as a specific MAA activator, we determined that the latter is true regardless of whether the employed anesthetic is a vasodilator (e.g., halothane)¹¹ or a vasoconstrictor (e.g., pentobarbital; Lanier and Iaizzo, unpublished data, 1995). Hence, one would anticipate that, in subjects with increased intracranial elastance and normal brain function (as might occur with a brain tumor), the setting would be optimal for stimulated increases in ascending afferent input causing an increase in ICP. In contrast, in a patient having increased intracranial elastance and severe global cerebral dysfunction (as might occur with severe head injury), the brain would have little or no response to increased ascending afferent input. In the latter setting, any increase in ICP accompanying movement² would be expected to result from a mechanism other than increased afferent-induced activation (e.g., passive venous congestion).

In conclusion, this study demonstrated that the ICP response to a noxious stimulus was related to skeletal muscle activation. However, increased CVP could only partially account for the ICP response. We also discovered in paralyzed dogs that only a fraction of the static increase in SVCP (one half or less) was transmitted to the cranium, resulting in increased ICP.

Assuming these observations in dogs are transferable to humans, we hypothesize that increased ICP during movement is due to two complementary factors: (1) cerebrovascular dilation that correlates with skeletal muscle activity⁵ and is mediated by proprioceptors, and (2) passive venous congestion that results from

any increased CVP or jugular venous pressure. The relative portions of these two factors will depend, in part, on the patient's baseline cerebral function, the depth of background anesthesia, and degree of elevation of the head.

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