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Effect of a Vecuronium-induced Partial Neuromuscular Block on Hypoxic Ventilatory Response

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Background: **A previous study has demonstrated a decrease in the hypoxic ventilatory response in volunteers partially paralyzed with vecuronium. However, in this study, hypocapnia was allowed to occur. Because hypocapnia counteracts the ventilatory response to hypoxia during partial vecuronium-induced neuromuscular block and isocapnia, the hypoxic ventilatory response (HVR) was tested in 10 awake volunteers.**

Methods: **To avoid hypocapnia, the resting hyperoxic control end-tidal P_{CO_2} was increased to 43.3 ± 2.4 mmHg, raising inspiratory minute ventilation ($\dot{V}_I$) to 140 ml · kg^{-1} · min^{-1}. Hypoxic ventilatory response ($\Delta\dot{V}_I/\Delta Sp_{O_2}$, L · min^{-1} · %$^{-1}$) was measured during a 5-min isocapnic step reduction to a mean arterial hemoglobin oxygen saturation (Sp_{O_2}) of 84.8 ± 1.4%. Immediately thereafter, hypercapnic ventilatory response (HCVR; $\Delta\dot{V}_I/\Delta P_{ET_{CO_2}}$, L · min^{-1} · mmHg^{-1}) was determined at the end of a 6-min step increase of $P_{ET_{CO_2}}$ to 50.5 ± 2.7 mmHg. During a subsequent 30–40-min pause, an intravenous infusion of vecuronium was adjusted to reduce the adductor pollicis train-of-four ratio to 0.70, as monitored using mechanomyography. Ventilatory parameters, HVR and HCVR, were then redetermined.**

Results: **Resting $\dot{V}_I$, $P_{ET_{CO_2}}$, and Sp_{O_2} were unchanged by drug infusion. Hypoxic ventilatory response decreased from control (a) of 0.97 ± 0.43 to 0.74 ± 0.41 L · min^{-1} · %$^{-1}$ ($P < 0.02$) during drug infusion (b), while HCVR was unchanged (a = 1.91 ± 0.82, b = 1.62 ± 0.46 L · min^{-1} · mmHg^{-1}; NS). To correct HVR for possible vecuronium-induced respiratory muscle weakness or otherwise altered central nervous system reactivity, the drug/control ratio ($HVR_{b/a}$) was divided by the associated $HCVR_{b/a}$ ratio. This HVR index, F_{HVR}, was 0.84 ± 0.12 ($P < 0.01$).**

Conclusions: **We conclude that a vecuronium-induced partial neuromuscular block impairs HVR more than it does HCVR in humans, suggesting an effect of vecuronium on carotid body hypoxic chemosensitivity. (Key words: Carbon dioxide: ventilatory response. Chemoreceptors, peripheral: carotid. Neuromuscular relaxants: vecuronium. Oxygen: hypoxic ventilatory response. Receptors: acetylcholine. Regulation of respiration.)**

IT has been widely accepted that recovery of the adductor pollicis muscle to a train-of-four (TOF) ratio of 0.70 is associated with respiratory muscle function adequate to permit safe tracheal extubation and spontaneous ventilation after nondepolarizing neuromuscular block.[1] However, the recovery characteristics from nondepolarizing neuromuscular blockade differ among muscle groups.[2] Residual weakness of pharyngeal muscles has been demonstrated after full recovery of the diaphragm.[3] Furthermore, in a recent study using a vecuronium infusion in awake volunteers,[4] ventilatory response to hypoxia was reported to be reduced without reduction in hypercapnic ventilatory response at a TOF ratio of 0.70, suggesting the possibility that vecuronium impairs hypoxic chemoreception. However, during hypoxic testing in that study, P_{CO_2} was not held constant. Such poikilocapnic hypoxic ventilatory tests provide limited information about hypoxic chemosensitivity because the hypoxic drive to increase ventilation is counteracted by the simultaneous reduction in medullary P_{CO_2} sensitive chemoreceptor drive with falling arterial P_{CO_2}.[5,6] Rebuck and Campbell,[7] applying their oximetric isocapnic hypoxic ventilatory response (HVR) test, have shown the importance of this O_2-CO_2 interaction. At a given arterial hemoglobin oxygen saturation, the increase in ventilation is 10–20 times greater with constant P_{CO_2} than during poikilocapnia.

Despite this caveat, the possibility that vecuronium might specifically depress hypoxic ventilatory response

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should be considered, since partial neuromuscular block is known to be associated with a considerable acetylcholine receptor occupancy.[8] Acetylcholine appears to be involved in carotid body chemoreceptor function during hypoxemia.[9-12] In addition, Bisgard *et al.* demonstrated in dogs that d-tubocurarine in subparalytic doses significantly reduced the sinus nerve hypoxic response over a range of arterial oxygen tensions.[13] Therefore, an isocapnic HVR study was planned to assess the effect of a vecuronium-induced partial neuromuscular block on the isocapnic HVR in awake human volunteers.

Subjects and Methods

The protocol was approved by the Human Research Committee of the University of California in San Francisco. A preliminary screening isocapnic HVR test was used to eliminate volunteers with less than 0.3 $L \cdot min^{-1} \cdot \%^{-1}$ sensitivity. Ten healthy volunteers of age 21–41 yr, height 177 ± 12 cm, and weight 77 ± 20 kg (6 men, 4 women) provided written informed consent. They were sea-level dwellers, nonsmokers, and without history of neuromuscular disorders and denied illegal drug use. Oral intake of caffeine or alcohol was not allowed for 12 h before the study, and subjects fasted for at least 6 h before entering the study.

Ventilatory Test Procedure

Subjects were studied while semi-supine with head and trunk elevated about 20°, and with eyes closed. An infusion of normal saline was given intravenously at 1–2 $ml \cdot kg^{-1} \cdot h^{-1}$ in the arm not used for neuromuscular monitoring. A comfortable anesthesia cushion mask was held over nose and mouth with headstraps. Ventilation was recorded as mean inspiratory flow ($\dot{V}_I$, L/min), using a 10-L open-tube rebreathing reservoir as recently described,[14] with a breathing valve (medium two-way, Hans Rudolph, Kansas City, MO) and pneumotachometer (#2 Fleisch®, Gould Godart, The Netherlands). From end-tidal P_{O_2} and P_{CO_2}, monitored with a Perkin Elmer MGA1100® mass spectrometer, an estimate of Sa_{O_2} termed Sc_{O_2} was computed on-line, displayed, and used for breath-by-breath adjustment of the inspired gas mixture to maintain steady-state isocapnia and hypoxia.[14] To minimize random errors in individual pulse oximeters, Sp_{O_2} was computed as the mean of three continuously recorded finger pulse oximeters (Nellcor N-100®, Ohmeda 3700®, and Criticare 504-US®). Oximeter probes were mounted on the hand not used for neuromuscular monitoring. Ventilation, saturation, and gas concentrations were recorded continuously for later computer analysis.

Definition of Hyperoxic Control (Resting) Ventilation

After subjects had rested for 10 min, while breathing an oxygen concentration of 40–45%, carbon dioxide was added to inspired gas to increase $\dot{V}_I$ to about 140 $ml \cdot kg^{-1} \cdot min^{-1}$. This was done to ensure that "resting" P_{CO_2} was sufficiently high to begin stimulating ventilation, reducing the problem of unrecognized hyperventilation due to anxiety or other "stressful" factors. After $\dot{V}_I$ had been stable for 5 min, this defined isocapnic $P_{ET_{CO_2}}$ level was maintained constant during the subsequent testing of HVR.

Measurement of HVR (Isocapnic Hypoxic Ventilatory Response)

The inspiratory oxygen fraction was decreased rapidly and adjusted to hold Sc_{O_2} at 80–85% while keeping $P_{ET_{CO_2}}$ constant by adding carbon dioxide to inspired air with a flowmeter. Hypoxic ventilatory response was then computed from mean $\dot{V}_I$ and Sp_{O_2} during the last 2 min of a 5-min hypoxic steady state, as:

$$HVR = \frac{\dot{V}_I^t - \dot{V}_I^c}{Sp_{r_{O_2}}^c - Sp_{O_2}^t}$$

where c and t refer to hyperoxic control and hypoxic test respectively. Whereas HVR is commonly reported as a negative number, the positive value obtained here as the ratio of changes of ventilation and desaturation avoids ambiguity inherent in describing a reduction of a negative value.

Measurement of Hypercapnic Ventilatory Response

Immediately after the hypoxic test, the inspiratory oxygen fraction was increased to >0.4 and carbon dioxide was added to inspired gas to rapidly increase $P_{ET_{CO_2}}$ by 6–10 mmHg and hold it constant for 6 min. Hypercapnic ventilatory response (HCVR) was calculated as the mean $\dot{V}_I$ during the last 2 min of this period, as:

$$HCVR = \frac{V_I^h - V_I^c}{P_{ET_{CO_2}}^h - P_{ET_{CO_2}}^c}$$

where c and h refer to the control and hypercapnic periods. The mask was then removed and the subject allowed to breathe room air.

This test sequence was repeated 30–40 min later during a stable neuromuscular block corresponding to a mechanical adductor pollicis TOF ratio of 0.70. The specific effects of vecuronium on HVR and HCVR were calculated as ratios of responses, $HVR_{b/a}$ and $HCVR_{b/a}$, where a and b refer to the control and vecuronium tests, respectively. F_{HVR}, an HVR index, was computed as $HVR_{b/a}/HCVR_{b/a}$ to estimate the specific effect of the vecuronium on hypoxic chemosensitivity. In concept, the concurrent changes in HCVR were used to correct the changes in HVR for any effects of vecuronium and time on respiratory muscles and changes of subject state such as drowsiness, anxiety, restlessness, and discomfort.

Control Group (Repeated HVR and HCVR Tests without Vecuronium)

To determine whether changes in HVR seen during vecuronium infusion might be due to a "second test effect" rather than to the vecuronium, the five subjects who showed the most reduction in HVR during vecuronium infusion were restudied 10 weeks later without administration of vecuronium. Ventilatory test procedures and experimental conditions were the same as in the previous testing, including continuous TOF ulnar nerve stimulation and 30 min between the tests. No intravenous infusion was given.

Neuromuscular Block

Neuromuscular transmission was evaluated using mechanomyography of the adductor pollicis muscle. The evoked twitch response was measured after supramaximal TOF ulnar nerve stimulation at the wrist (0.3-ms square pulses at 2 Hz for 2 s every 12 s) using a Myotest® nerve stimulator (Biometer, Odense, Denmark). Mechanical TOF responses were recorded using a Myograph 2000® neuromuscular transmission analyzer (Biometer). A stable baseline recording was established during an initial 10–15 min of single-twitch 1-Hz stimulation. Thereafter the twitch response was recorded continuously during TOF stimulation given every 12 s throughout the study. A preload of 0.25–0.30 kg was maintained on the thumb, and it was repeatedly confirmed that the nerve stimulation was supramaximal. The TOF response of all subjects returned to control response after spontaneous recovery from neuromuscular block. Skin temperature over the adductor pollicis muscle was continuously measured (Surface Probe model 1800, Sensortek®, Clifton, NJ) and was maintained above 32° C by covering the arm with a warming blanket.[15]

Vecuronium was administered as a continuous infusion (5 mg Norcuron® diluted in 50 ml of normal saline, *i.e.*, 0.1 mg/ml) in the arm not used for neuromuscular monitoring, using a motor-driven syringe (Medfusion® 1001, Medex, Atlanta, GA). The infusion rate was adjusted to establish and maintain a neuromuscular block at a TOF ratio of approximately 0.70. During steady-state neuromuscular block, the height of the first twitch in the TOF response was >90% of control in all subjects. The total dose of vecuronium given was 33 ± 8 μg/kg (mean ± SD) over about 30 min.

Statistics

Significance of the differences from 1.00 of the ratios $HVR_{b/a}$, $HCVR_{b/a}$, and index F_{HVR}, and other changes from test a to b were determined using Student's paired *t* test. A *P* value of less than 0.05 was considered statistically significant.

Results

Test Group

Resting mean $\dot{V}_I$, $P_{ET_{CO_2}}$, and Sp_{O_2} were unchanged during infusion of vecuronium (table 1), and the mechanical TOF ratios during infusion of vecuronium were the same during measurements of HVR and HCVR (table 2).

Table 1. Mean ± SD of Inspiratory Minute Ventilation ($\dot{V}_I$), Pulse Oximetric Arterial Oxygen Saturation (Sp_{O_2}), and End-tidal Carbon Dioxide Tension ($P_{ET_{CO_2}}$) of 10 Subjects during the Control (Rest) Period, at the End of 5 min of Isocapnic Hypoxia, and at the End of 6 min of Hyperoxic Hypercapnia before and during Vecuronium-induced Partial Neuromuscular Block

	Rest	Hypoxia	Hypercapnia
$\dot{V}_I$ (L/min)			
Before	10.1 ± 1.4	23.9 ± 5.7	23.3 ± 5.5
During	10.4 ± 2.3	21.2 ± 6.9	22.0 ± 5.8
Sp_{O_2} (%)			
Before	99.2 ± 0.5	84.8 ± 1.4	99.1 ± 0.4
During	99.1 ± 0.5	84.4 ± 1.6	99.1 ± 0.4
$P_{ET_{CO_2}}$ (mmHg)			
Before	43.3 ± 2.4	43.2 ± 2.3	50.5 ± 2.7
During	43.4 ± 2.8	43.2 ± 2.4	50.6 ± 3.3

Table 2. Hypoxic Ventilatory Responses (HVR, $L \cdot min^{-1} \cdot \%^{-1}$), Hypercapnic Ventilatory Responses (HCVR, $L \cdot min^{-1} \cdot mmHg^{-1}$), and the Ratios of Each during (Vecuronium Infusion) (b) to Control (a)

Subject No.	HVR		HCVR					TOF	
	a	b	a	b	$HVR_{b/a}$	$HCVR_{b/a}$	F_{HVR}	Hypoxia	Hypercapnia
1	1.54	1.16	2.45	2.23	0.76	0.91	0.83	0.67	0.68
2	1.16	0.68	2.93	2.17	0.58	0.74	0.79	0.70	0.72
3	1.00	0.68	1.78	1.02	0.66	0.57	1.16	0.71	0.72
4	1.78	1.56	1.35	1.45	0.88	1.07	0.82	0.70	0.70
5	0.89	0.71	2.17	1.90	0.79	0.87	0.91	0.72	0.70
6	0.40	0.35	0.77	0.84	0.88	1.09	0.81	0.67	0.68
7	0.87	1.13	1.18	1.87	1.30	1.59	0.81	0.78	0.74
8	0.53	0.36	1.88	1.66	0.69	0.88	0.78	0.72	0.66
9	0.62	0.45	1.28	1.32	0.72	1.03	0.71	0.71	0.70
10	0.94	0.38	3.34	1.77	0.40	0.53	0.75	0.72	0.83
Mean	0.97	0.74	1.91	1.62	0.77	0.93	0.84	0.71	0.70
SD	0.43	0.41	0.82	0.46	0.23	0.30	0.12	0.03	0.03
P					0.012	0.47	0.002		

F_{HVR} = ratio of these ratios, $HVR_{b/a}/HCVR_{b/a}$ taken as an index of the specific effect of vecuronium on HVR (via peripheral chemoreceptors); TOF = the index of neuromuscular block; the train-of-four ratio (T4:T1).
$P < 0.05$ indicates the ratio is different from 1.00.

The changes of HVR and HCVR observed during vecuronium infusion were closely correlated (r = 0.94; fig. 1). There was no correlation between the control values of HVR *versus* HCVR.

The individual and mean HVR and HCVR data during control and vecuronium infusion states are presented in table 2. During vecuronium-induced partial neuromuscular block, mean HVR decreased by 23% (*P*

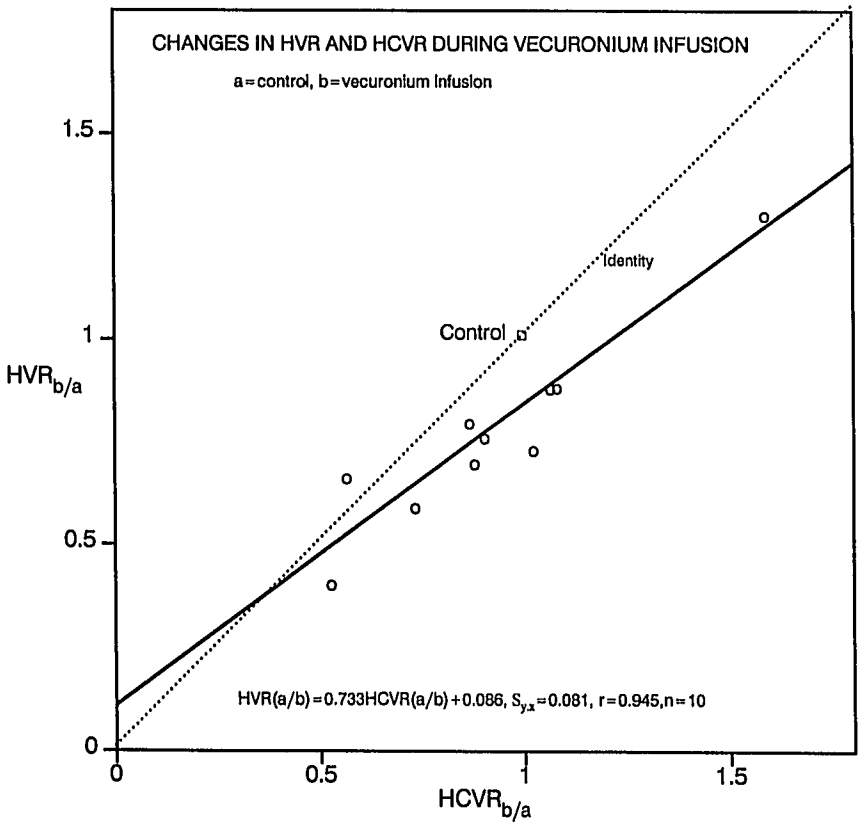

Fig. 1. Changes of hypoxic ventilatory response (HVR) and hypercapnic ventilatory response (HCVR) from control (a) to vecuronium infusion at train-of-four ration of 0.70 (b), described as ratios $HVR_{b/a}$ and $HCVR_{b/a}$, showed wide intersubject variability, but were significantly correlated, suggesting that muscle weakness reduced the two responses proportionally. In one anxious subject, both were proportionally increased.

< 0.02), whereas HCVR did not change significantly. Nine subjects showed reduced HVR (range 12–60% reduction). The index F_{HVR} was 0.84 ± 0.12 ($P = 0.002$). One subject, who was anxious, showed an increase of both HVR and HCVR. Exclusion of this subject yielded: mean $HVR_{b/a} = 0.71 \pm 0.15$ ($P < 0.001$), $HCVR_{b/a} = 0.86 \pm 0.23$ (NS), and $F_{HVR} = 0.84 \pm 0.13$ ($P < 0.001$). Conclusions were unaltered.

All subjects reported diplopia and exhibited ptosis at a TOF ratio of 0.70. In addition, three subjects complained of difficulty swallowing. Frequency of complaints was the same during HVR and HCVR tests. None of the subjects reported weakness or discomfort before infusion of vecuronium or after full recovery of the TOF response.

Control Group

In the five subjects (2, 3, 8, 9, and 10) retested later without neuromuscular block, there was no significant difference of HVR, HCVR, or F_{HVR} between the first and second measurements separated by 30 min (tables 3 and 4).

Discussion

This study confirms the previous test[4] of the hypothesis that vecuronium-induced partial neuromuscular block at a TOF ratio of 0.70 specifically reduces the ventilatory response to isocapnic hypoxia without altering the response to hypercapnia.

There remains some controversy regarding the general view supported by early findings of Ali *et al.*[1] that recovery of the adductor pollicis TOF ratio to 0.70 after nondepolarizing neuromuscular blocking agents is associated with normal vital capacity, tidal volume, and end-tidal carbon dioxide tension at rest, and recovery of maximal inspiratory muscle force. Recovery of pharyngeal and other upper airway muscles occurs after diaphragmatic recovery.[2,3] Other studies during partial neuromuscular block in awake humans have shown that the ventilatory response to increased $P_{ET_{CO_2}}$ is well maintained despite considerable weakness of peripheral hand muscles.[4,16,17] Confirming this, we were unable to find a significant change of either isocapnic resting ventilation or HCVR during a partial neuromuscular block. Thus, in unloaded respiratory muscles of awake nonanesthetized humans, the ventilatory response to hypercarbia and ventilatory capacity do not appear significantly impaired by vecuronium at an adductor pollicis TOF ratio of 0.70.

Table 3. Test of the Repeatability of HVR and HCVR in the Absence of Vecuronium in the 5 Subjects Who Had the Greatest Reduction of HVR during Infusion of Vecuronium

	Test	Rest	Hypoxia	Hypercapnia
$\dot{V}_I$ (L/min)	1	10.2 ± 0.9	26.5 ± 9.1	28.2 ± 5.0
	2	10.5 ± 0.9	28.1 ± 7.7	30.6 ± 6.7
Sp_{O_2} (%)	1	99.3 ± 0.2	80.2 ± 3.2	99.4 ± 0.5
	2	99.6 ± 0.3	81.0 ± 2.0	99.5 ± 0.2
$P_{ET_{CO_2}}$ (mmHg)	1	41.8 ± 3.7	42.6 ± 3.7	50.5 ± 4.0
	2	42.3 ± 3.3	42.2 ± 23.4	52.3 ± 3.1

Tests 1 and 2 were separated by 30 min of rest breathing air.

Table 4. Individual and Mean Data of the Test of the Repeatability of HVR and HCVR in the Absence of Vecuronium in the 5 Subjects Who Had the Greatest Reduction of HVR during Infusion of Vecuronium

Subject No.	HVR		HCVR				
	Test 1	Test 2	Test 1	Test 2	$HVR_{2/1}$	$HCVR_{2/1}$	F_{HVR}
2	0.84	1.12	2.55	2.69	1.33	1.05	1.26
3	0.54	0.80	1.47	1.05	1.48	0.71	2.08
8	0.28	0.36	0.91	1.63	1.27	1.78	0.71
9	0.98	0.88	1.09	1.52	0.90	1.39	0.65
10	1.44	1.70	3.08	4.19	1.18	1.36	0.86
Mean	0.81	0.97	1.82	2.22	1.23	1.25	1.11
SD	0.43	0.49	0.94	1.25	0.21	0.40	0.59
					NS	NS	NS

Carotid Body and Neuromuscular Blocking Drugs

Some nondepolarizing neuromuscular blocking agents (*e.g.*, d-tubocurarine) have been shown to reduce nerve discharge from carotid body during hypoxia in animals, the reduction being reversed by administration of acetylcholine esterase inhibitors.[10] Furthermore, acetylcholine is believed to modulate the hypoxic chemoreceptor response in association with dopamine.[9–11] Interestingly, Bisgard et al.[13] found in dogs a 14–49% reduction of isocapnic hypoxic response of carotid body chemoreceptor nerve discharge after partial or complete d-tubocurarine-induced block, but no reduction of the response after gallamine or succinylcholine.

Chemoreceptor cells of the carotid body have nicotinic and muscarinic acetylcholine reactive sites, the chemoreceptor cell membrane being depolarized by agonists (*e.g.*, nicotine or pilocarpine), the agonist response being counteracted by administration of antagonists (*e.g.*, d-tubocurarine or atropine).[12] Our findings in humans are thus supported by animal studies show-

ing that neuromuscular blocking agents impair carotid body function during hypoxia.

Diaphragm Versus *Thoracic Muscle Sensitivity*

It might be reasoned that the observed effect of vecuronium on HVR, greater than on HCVR, was caused by a differential effect on the respiratory muscles involved in responses to hypoxia *versus* hypercapnia. Hypoxic drive is associated with relatively more diaphragmatic drive, whereas the hypercapnic response depends on diaphragm and thoracic muscles about equally.[18] However, the diaphragm is known to be more resistant than other respiratory muscles to nondepolarizing neuromuscular blocking agents.[2,3] It is therefore unlikely that the reduced HVR was caused by selective diaphragmatic muscle weakness. Furthermore, the infusion rate of vecuronium was adjusted to establish and maintain TOF fade without a simultaneous reduction of the T1 twitch height. This was achieved in all subjects, and the relationship between the degree of fade and reduction of twitch height was therefore close to that seen during recovery from a neuromuscular block.

Artifacts and Errors in HVR Testing

Subjects with low HVR were excluded from this study. A normal population of young healthy individuals will include subjects with a very low response to isocapnic hypoxia. Exclusion of such individuals may have increased the observed effect if high sensitivity to hypoxia involves a more important role for acetylcholine in the carotid body.

Hypoxic ventilatory response measurement has been shown to be independent of the oxygen saturation used in testing (at least over the range 70–85% Sa_{O_2}).[7,14] Although the mean Sp_{O_2} was about 4% lower during both of the repeat control tests (table 3) than during the original tests (table 1), the mean HVR of those five subjects in the initial study was not different from their mean when retested. The reproducibility of HVR in individual subjects for tests separated by 10 weeks, with the tests performed by different investigators, was poor ($r = 0.33$).

Hypercapnic ventilatory response was measured to correct for possible respiratory muscle weakness during vecuronium infusion. Although there was a large range of change of HCVR of approximately ±50% as well as HVR associated with the infusion of vecuronium, the mean HCVR was not significantly reduced. Thus, the changes may have been related to factors such as anxiety, which proportionally altered both HVR and HCVR. One of these 10 subjects, who became anxious (as manifested by pallor, sweating, and restlessness), showed increased HVR and HCVR during vecuronium infusion. Nevertheless, his index F_{IIVR} was 0.81, comparable to the mean F_{IIVR} of the other nine subjects, 0.84. Since there is no direct evidence that these side effects have equal impact on HVR and HCVR, the indexing of ΔHVR to ΔHCVR may be inappropriate.

Isocapnia in terms of testing ventilatory response usually means maintaining $P_{ET_{CO_2}}$ at the resting level found while breathing ambient air. However, volunteers may be hyperventilating slightly when "resting P_{CO_2}" is measured, and a below-normal P_{CO_2} will reduce the measured HVR. When breathing air at rest, most awake individuals have a rather flat initial portion of the carbon dioxide response curve, often called the "dog-leg," suggesting that the central chemoreceptor drive may not be the only ventilatory drive present. This flat region is less evident during hyperoxia[5,6] and may be avoided by choosing a "resting" P_{CO_2} sufficiently elevated to demonstrably begin to stimulate ventilation. When HVR is tested repeatedly, this has the added advantage of performing all tests with the same central chemoreceptor drive level, rather than at the same $P_{ET_{CO_2}}$, which varies with time of day and many other factors. Although in using elevated resting P_{CO_2} we expected above-normal HVR, our mean of 0.97 $L \cdot min^{-1} \cdot \%^{-1}$ compares well with the normal mean HVR of 1.0 $L \cdot min^{-1} \cdot \%^{-1}$ given by Rebuck and Campbell.[7]

After about 5 min of isocapnic hypoxia, $\dot{V}_I$ begins to decrease because of hypoxic ventilatory depression and stabilizes after about 30 min, losing about half the hypoxic increment.[19,20] Hypoxic ventilatory depression may alter the measured HVR if the test procedure lasts more than 5 min. Moreover, HVR will remain depressed if retested within 7–15 min of subsequent normoxia but will be normalized by 7 min of inspiratory oxygen fraction of 1 or 20–30 min breathing air.[20] Therefore, we have completed each HVR test within 5 min of hypoxia and have separated HVR tests by 30–40 min. The control studies of the five subjects exhibiting the greatest fall with vecuronium excluded the possibility that the second test (with or without drug) was reduced by residual hypoxic ventilatory depression. Neither hypoxia nor hypercapnia during their brief administrations had any detectable effect on muscle strength, as monitored by testing of TOF response (table 2), since no

change in vecuronium infusion rate was needed during these tests.

We conclude that a vecuronium-induced partial neuromuscular block impairs HVR more than HCVR in humans, suggesting an effect of vecuronium on carotid body hypoxic chemosensitivity.

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