α2-Adrenergic modulation of colonic tone during hyperventilation

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Bharucha, Adil E., Vera Novak, Michael Camilleri, Alan R. Zinsmeister, Russell B. Hanson, and Phillip A. Low. α2-Adrenergic modulation of colonic tone during hyperventilation. Am. J. Physiol. 273 (Gastrointest. Liver Physiol. 36): G1135–G1140, 1997.—Our aims were to assess the role of adrenergic modulation in the hyperventilation-induced increase in colonic tone. Of 40 healthy volunteers, 12 received placebo (saline) and the remaining 28 received either clonidine, yohimbine, phentolamine, or metaraminol. Time-frequency mapping of heart rate based on Wigner distribution assessed variations in parasympathetic and sympathetic activity during hyperventilation. Tone in the descending colon was recorded by a barostat balloon before, during, and after 5 min of hyperventilation. Heart rate spectral analysis suggested diminished sympathetic and vagal activity during hyperventilation and increased sympathetic and vagal activity after hyperventilation. Adrenergic agents influenced (P = 0.01) the tonic response after, but not during, hyperventilation. Yohimbine reduced the increment in colonic tone after hyperventilation compared with saline (P < 0.05) and clonidine (P = 0.002); phentolamine and metaraminol had no effects. Different mechanisms modulate the increase in colonic tone during and after hyperventilation. Yohimbine attenuates the increase in colonic tone after hyperventilation probably by enhancing inhibitory sympathetic input to the colon.

Previous work has shown that colonic tone increases during and immediately after hypocapnic hyperventilation in healthy volunteers (2, 8). Hypocapnic hyperventilation changes autonomic tone and can be used as a model to evaluate control of colonic motor function in humans. Hyperventilation is associated with stress (27) and was shown to increase perception of colonic distension (2) in humans.

The mechanisms responsible for the colonic effects of hyperventilation are unclear. Eucapnic hyperventilation, performed by inhaling 5% CO2 during hyperventilation, does not increase colonic tone (8). Thus hypocapnia is necessary to elicit this response, possibly by a direct effect of hypocapnia on colonic muscle or by neural modulation (2).

In several species, including humans, the sympathetic nervous system exerts a primarily α1-mediated tonic inhibitory effect on gastrointestinal motor function (17). α2- and β2-adrenergic receptors also reduce colonic contractile frequency in nonhuman primates (21). In a previous study, indexes of sympathetic activity were unchanged during hyperventilation. After hyperventilation, a rise in plasma norepinephrine was accompanied by a fall in splanchnic blood volume, suggesting a homeostatic response in central circulation or resetting of autonomic neural control after the cessation of hyperventilation (2).

To further assess the neural mechanisms responsible for the increase in colonic tone induced by hyperventilation, we pharmacologically modulated sympathetic activity at α2- and β2-receptors. We simultaneously monitored the heart rate and performed spectral analysis to identify alterations in parasympathetic and sympathetic modulation to the heart as a surrogate of autonomic function. Power spectral analysis of heart rate quantifies short-term fluctuations of heart rate, which represent changing levels of autonomic control of the sinoatrial node (24). The heart rate power spectrum normally presents a peak at the respiratory frequency >0.1 Hz, which represents respiratory sinus arrhythmia, and other peaks at lower frequencies between 0.01 and 0.1 Hz. Whereas fluctuations at respiratory frequencies >0.1 Hz are mediated solely by modulation of parasympathetic outflow, fluctuations at lower frequencies (0.01–0.1 Hz) are mediated by modulation of both the parasympathetic and sympathetic inputs to the sinoatrial node.

Materials and Methods

Healthy Volunteers

Forty healthy volunteers, aged 18–45 yr (mean ± SE, 29 ± 1.1 yr; 22 males and 18 females), were recruited by public advertisement. None had previously undergone abdominal surgery (other than an appendectomy and/or cholecystectomy). A clinical interview and physical examination were performed and none of the subjects were on medications that influence gastrointestinal motility or autonomic function. Validated screening questionnaires [The Bowel Disease Questionnaire (26) and The Hospital Anxiety and Depression Inventory (28)] were used to exclude subjects with irritable bowel syndrome and to determine anxiety and depression scores. All participants signed informed consent forms to participate in the studies, which were approved by the Institutional Review Board at the Mayo Clinic.

Administration of Drugs

Because of human safety considerations, the subject, but not the investigator, was blinded to the nature of the medication. Subjects were informed that they would be randomized to either a medication or placebo, administered either intravenously or orally. As control or placebo, we administered 10 ml 0.9% saline as a bolus over 5 min, followed by an infusion at 40 ml/h. The bolus volume and rate of administration were similar for yohimbine, the only other agent administered as a bolus followed by an infusion.

Clonidine. Clonidine (0.3 mg; Zenith, Northvale, NJ) was given as a single oral dose after fasting colonic tone had been assessed for at least 20 min. This dose has previously been
demonstrated to slow intestinal and colonic transit and to enhance fluid absorption in healthy volunteers for at least 4.5 h (22). Intravenous clonidine is not available for administration to humans in the United States. However, the bioavailability of oral clonidine is nearly 100%; peak concentrations and maximal antihypertensive effects are achieved at 1–3 h after oral administration (10), which coincides with the planned experimental protocol in our studies. Pharmacodynamic observations in our studies confirmed these findings with an obvious effect on colonic motor function after the systemic blood pressure had declined by $\geq 10$ mmHg, usually 40–55 min after the 0.3-mg dose had been administered orally.

Yohimbine hydrochloride. An intravenous formulation of yohimbine is not available in the United States. We obtained Investigational New Drug no. 46,250 from the Food and Drug Administration to use an aqueous-based solution of yohimbine, prepared by the Mayo Clinic Pharmacy from yohimbine hydrochloride (Sigma Chemical, St. Louis, MO). Stability of the aqueous solution of yohimbine over the 6-mo period required to complete the study was checked by periodic high-performance liquid chromatographic analysis. Yohimbine was administered as an initial 0.125 mg/kg iv bolus over 5 min followed by an infusion at 0.06 mg·kg$^{-1}$·h$^{-1}$. Yohimbine is used clinically to provoke panic attacks in patients with a history of panic disorder (1), and a similar dosing regimen stimulates central sympathetic output and results in a two- to threefold increase in plasma norepinephrine levels (9). The effects of yohimbine on heart rate spectral analysis at rest were assessed during the intravenous infusion, and not the bolus.

Phenylephrine. Phenylephrine (Elkins-Sinn, Philadelphia, PA), a selective $\alpha_1$-agonist, causes peripheral vasoconstriction, thereby increasing blood pressure and inducing reflex bradycardia. An initial dose of 0.4 µg·kg$^{-1}$·min$^{-1}$ iv was titrated upward in 0.4 µg·kg$^{-1}$·min$^{-1}$ increments at 10-min intervals until the systolic blood pressure increased by 20 mmHg or until a maximum infusion rate of 2.5 µg·kg$^{-1}$·min$^{-1}$ was achieved. For a 70-kg person, the median maximum dose of 84 µg/min (range 70–140 µg/min) was in the range recommended (40–180 µg/min) for treating hypotension in conditions such as hypovolemic or septic shock (15).

Ritodrine. Ritodrine (Abbott, Abbott Park, IL), a selective $\beta_2$-agonist, was infused intravenously at an initial dose of 50 µg/min, increasing by 50 µg/min at 10-min intervals until the heart rate had increased by 50% or a maximum dose of 300 µg/min was reached. The dose range of 50–300 µg/min and the dosing regimen are similar to that recommended for inhibiting uterine contractions in preterm labor, that is, 150–350 µg/min (16).

For phenylephrine and ritodrine, the same dose was maintained during the entire period of this study. The effects of phenylephrine and ritodrine on fasting colonic motor function and heart rate were measured for 20 min after the target systolic blood pressure and heart rate were achieved.

Hemodynamic Monitoring

We continuously monitored arterial oxygen saturation, blood pressure, and cardiac rhythm using a pulse oximeter (CO2SMO, Novametrix Medical Systems, Wallingford, CT), Finapres sphygmonanometry (Ohmeda, Madison, WI), and electrocardiogram (ECG; Tektronix, Beaverton, OR), respectively. The blood pressure measurements were also confirmed by standard manual sphygmonanometry at regular intervals during the study.

Spectral Analysis of Heart Rate

The spectral analysis of heart rate was conducted for 10-min segments before and after drug administration and for 5 min during and after hyperventilation. Indexes of parasympathetic and sympathetic functions were based on oscillations of the R-R interval at respiratory (RF, >0.1 Hz) and nonrespiratory frequencies (non-RF, 0.01–0.09 Hz). The time-frequency mapping process is based on a modified Wigner distribution and decomposes the signal as a function of time into a function of time and frequency (18, 19). High resolution was achieved by an independent time and frequency smoothing (18). Before computation of the Wigner distribution, extrasystoles and outlying values were removed from the raw data. The time series of R-R intervals were linearly interpolated and resampled at 2 Hz, as is required for spectral estimation. The low-frequency baseline trend was removed using a polynomial function from cross-Wigner distribution. RF fluctuations in R-R intervals were detected according to the breathing frequency over a wide range (0.1–0.5 Hz), and non-RF fluctuations were detected in the 0.01–0.09-Hz range with time resolution of 1 s.

Colonic Motor Function

A polyethylene balloon mounted on a multilumen assembly was placed into the prepared upper descending colon as described in previous studies with the aid of fluoroscopy (2). Tonic activity of the colon was monitored continuously as the baseline pressure (2, 25) in an infinitely compliant, 10-cm-long balloon. The maximum volume of the balloon was 600 ml (Hefty Baggies, Mobil Chemical, Pittsford, NY), and an electronic barostat (Distender Series II, G & J Electronics, Toronto, Canada) maintained constant pressure within the balloon. The intraball pressure at which respiratory excursions were regularly recorded as changes in barostat volume was defined as the minimum distending pressure. The operating pressure was set 2 mmHg above the minimum distending pressure (median pressure 10 mmHg, range 6–14 mmHg). A pneumobelt around the abdominal wall at the level of the costal margin helped to identify artifact during movement and coughing.

Hyperventilation

The method for inducing voluntary hyperventilation was similar to that used extensively in previous studies (2, 8). In the absence of pulmonary disease, the end-tidal Pco$_2$ level provides an accurate breath-by-breath estimate of the arterial Pco$_2$ level. The end-tidal Pco$_2$ level was measured continuously, using a nasal airflow sensor and standard capnography (CO2SMO). Patients were asked to hyperventilate at 30 breaths/min, using a mouthpiece and a metronome, so that the end-tidal Pco$_2$ level was maintained at $<26$ mmHg for 5 min. Colonic tone was assessed over 5-min periods before, during, and after hyperventilation.

Experimental Design

The experimental design is demonstrated in Fig. 1. All subjects were admitted to the General Clinical Research Center at St. Mary’s Hospital (Rochester, MN) on the evening before the study for bowel preparation, which comprised 1.5–2 liters of polyethylene glycol and electrolyte solution (oral colonic lavage solution; Abbott Laboratories, North Chicago, IL). This solution was drunk until the fecal effluent became a clear liquid. All volunteers signed informed consent forms and had a screening ECG to exclude significant rhythm disturbances or ischemia; women of childbearing potential
underwent a plasma β-human chorionic gonadotropin pregnancy test within 48 h of the studies. After an overnight fast, all subjects underwent left-sided colonoscopy without sedation. In the absence of any endoscopic abnormality, a 4-mm Teflon-coated guide wire (Microvasive, Hobbs Medical, Stafford Springs, CT) was placed with its tip at the splenic flexure, and the colon was deflated as the colonoscope was withdrawn. The balloon assembly was introduced into the colon over the guide wire and positioned under fluoroscopic control with the balloon in the mid-descending colon. The barostat balloon was inflated to operating pressure after a 30-min equilibration period. After another 30-min equilibration period, we began recording fasting colonic tone. Drug effects on fasting colonic tone were recorded for 20 min before and for 20 min after drug administration. For volunteers randomized to clonidine, the average interval between administration of the tablet and onset of recording postdrug colonic tone and ECG was 40 min. Similarly, for phenylephrine and ritodrine, we recorded the postdrug colonic tone and ECG for 20 min only after preset hemodynamic endpoints were achieved.

Data Analysis

Colonic motor parameters. Pressure and volume in the barostat balloon were sampled as analog signals at 8 Hz and converted to digital signals before entry into a computer. As in previous studies, movement and respiratory artifact were filtered out using a modified VAX Lab filtering program (Digital Equipment, Boston, MA [2,8]).

Phasic volume peaks recorded by the barostat balloon in the colon occur at a frequency of 3 peaks/min (25); the waveform was filtered to remove frequencies >6 peaks/min, and the barostat balloon volume was then computer analyzed to separate baseline balloon volume, representing colonic tone, from phasic volume events. Phasic volume events were defined as changes in volume ≥10 ml from baseline volume.

The balloon volume data were summarized over 20 min before and 20 min after drug administration, and for 5 min during and 5 min after hyperventilation. Balloon volume after drug administration was also used as the prehyperventilation balloon volume.

Statistical Analysis

The statistical analysis of colonic tone (barostat volume) and heart rate spectral parameters [R–R interval, spectral power at RF (RFmax), and spectral power at non-RF (non-RFmax)] involved three steps. First, to assess the effects of hyperventilation on colonic tone and heart rate spectral response in the placebo group, we used a paired t-test to compare postdrug (i.e., prehyperventilation) to hyperventilation, and prehyperventilation to posthyperventilation. Second, in an overall analysis of covariance (ANCOVA), we compared the differences (value during hyperventilation minus value prehyperventilation; value after hyperventilation minus value prehyperventilation) to determine if the adrenergic agents modified the heart rate spectral response or colonic tonic response either during or after hyperventilation after adjusting for differences between groups at baseline (predrug). Third, if the differences between drugs were statistically significant in the overall ANCOVA, we examined pairwise comparisons between placebo and clonidine, placebo and yohimbine, placebo and phenylephrine, placebo and ritodrine, and clonidine and yohimbine, using a P value adjusted for five statistical comparisons (i.e., P ≤ 0.01) for statistical significance. All data are shown as means ± SE.

RESULTS

In the 40 studies performed, technical problems (signal noise, frequent heart ectopy, or computer storage failure) precluded optimum spectral analysis of heart rate in seven volunteers and of colonic tone in two volunteers. Of these seven volunteers, two each were randomized to yohimbine and ritodrine, and three were randomized to phenylephrine. The arterial PCO2 decreased from 41 ± 0.8 mmHg (baseline) to 26 ± 0.6 mmHg during hyperventilation and increased to 31 ± 0.7 mmHg after hyperventilation.

Effect of Drugs on Heart Rate and Spectral Analysis of Heart Rate

Before hyperventilation, the adrenergic agents had a significant overall effect on the heart rate (P = 0.0001). Pairwise comparisons with placebo indicate that phenylephrine caused a reflex bradycardia (P < 0.001 adjusted for 5 tests), whereas ritodrine significantly increased heart rate (P < 0.001, adjusted for 5 tests, Table 1).

The heart rate increased significantly during hyperventilation (P < 0.0001) and returned to baseline

<table>
<thead>
<tr>
<th>Drug</th>
<th>Predrug</th>
<th>Postdrug</th>
<th>During hyperventilation</th>
<th>After hyperventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>987 ± 47</td>
<td>976 ± 45</td>
<td>796 ± 45*</td>
<td>989 ± 43</td>
</tr>
<tr>
<td>Clonidine</td>
<td>934 ± 47</td>
<td>969 ± 68</td>
<td>787 ± 74</td>
<td>973 ± 62</td>
</tr>
<tr>
<td>Yohimbine</td>
<td>1,036 ± 93</td>
<td>954 ± 78</td>
<td>802 ± 74</td>
<td>947 ± 94</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>921 ± 75</td>
<td>1,256 ± 28†</td>
<td>934 ± 97</td>
<td>1,253 ± 41</td>
</tr>
<tr>
<td>Ritodrine</td>
<td>963 ± 63</td>
<td>588 ± 28</td>
<td>472 ± 21</td>
<td>543 ± 25</td>
</tr>
</tbody>
</table>

Values are means ± SE. *P < 0.0001 vs. postdrug (i.e., prehyperventilation) placebo value by paired t-test. †P < 0.001 vs. placebo postdrug value.
immediately after hyperventilation for volunteers in the placebo group (Table 1). There were no significant drug effects on the differences in heart rate during or after hyperventilation. In the placebo group, there was a decline in the spectral peak in the non-RF range during hyperventilation (\(P < 0.04\)) and an increase of non-RF after hyperventilation (\(P < 0.04\)). Figure 2 depicts a significant overall drug effect on cardiac rhythm periodicity as shown by the power of the spectral peak in the non-RF range. This drug effect was noted before hyperventilation (\(P < 0.05\)) and after hyperventilation (\(P < 0.05\)), but not during hyperventilation. Phenylephrine significantly increased the non-RF peak during baseline (i.e., before hyperventilation; \(P < 0.05\), adjusted for 5 tests) but had no effect relative to the placebo group during or after hyperventilation.

\(RF_{\text{max}}\) decreased during hyperventilation (\(P < 0.01\)) and tended to increase after hyperventilation (\(P = 0.14,\) adjusted for 5 tests). In the 5-min epoch immediately after hyperventilation, tone increased by an additional 12\(\pm 6\) ml over hyperventilation (\(P < 0.001\) vs. hyperventilation, Fig. 4). The adrenergic agents did not modify the colon’s tonic response during hyperventilation. In contrast, an overall drug effect on the change in colonic tone after hyperventilation compared with prehyperventilation was observed. Phenylephrine significantly (\(P < 0.05\), adjusted for 5 tests) increased the spectral peak at RF before hyperventilation compared with placebo.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Barostat Volume, ml</th>
<th>During hyperventilation</th>
<th>After hyperventilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>76 (\pm 8)</td>
<td>69 (\pm 8)</td>
<td>57 (\pm 9^*)</td>
</tr>
<tr>
<td>Clonidine</td>
<td>83 (\pm 14)</td>
<td>131 (\pm 23^*)</td>
<td>121 (\pm 25)</td>
</tr>
<tr>
<td>Yohimbine</td>
<td>80 (\pm 12)</td>
<td>64 (\pm 13)</td>
<td>56 (\pm 11)</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>52 (\pm 8)</td>
<td>57 (\pm 11)</td>
<td>41 (\pm 10)</td>
</tr>
<tr>
<td>Ritodrine</td>
<td>64 (\pm 9)</td>
<td>80 (\pm 14)</td>
<td>67 (\pm 13)</td>
</tr>
</tbody>
</table>

Values are means \(\pm SE\). *\(P = 0.001\) vs. postdrug (i.e., prehyperventilation) placebo; †\(P = 0.001\) vs. during-hyperventilation placebo; ‡\(P = 0.02\) vs. postdrug placebo; §\(P < 0.05\) for the difference (after hyperventilation value minus postdrug (i.e., prehyperventilation) value) vs. this difference for placebo.

Fig. 3. A significant overall drug effect on the spectral powers at RF before hyperventilation (\(P < 0.05\)) but not during hyperventilation or after hyperventilation was observed. Phenylephrine significantly (\(P < 0.05\), adjusted for 5 tests) increased the spectral peak at RF before hyperventilation compared with placebo.

Effect of Adrenergic Agents on Colonic Tone at Rest and During and After Hyperventilation

Drug effects on fasting colonic tone have been presented in detail elsewhere (3) and are summarized in Table 2. Compared with saline, the \(\alpha_2\)-agonist clonidine significantly reduced baseline colonic tone. For volunteers randomized to receive placebo, colonic tone increased by 12\(\pm 3\) ml during hyperventilation (\(P = 0.001\) vs. prehyperventilation, Fig. 4). In the 5-min epoch immediately after hyperventilation, tone increased by an additional 12\(\pm 4\) ml over hyperventilation (\(P = 0.001\) vs. hyperventilation, Fig. 4).

The adrenergic agents did not modify the colon’s tonic response during hyperventilation. In contrast, an overall drug effect on the change in colonic tone after hyperventilation compared with prehyperventilation was observed. Phenylephrine significantly (\(P < 0.05\), adjusted for 5 tests) increased the spectral peak at RF before hyperventilation compared with placebo.

Fig. 4. Effect of drugs on colonic tonic motor response during and after HVT. Histograms depict increase in colonic tone (means \(\pm SE\)) during and after HVT compared with before HVT, after adjusting for differences between groups at baseline (i.e., predrug). *\(P < 0.05\), Yoh vs. placebo after HVT; †\(P = 0.01\), Yoh vs. Clo after HVT.
was observed ($P = 0.01$). Yohimbine significantly attenuated the increase in colonic tone after hyperventilation compared with saline ($P < 0.05$, adjusted for 5 tests). Moreover, clonidine and yohimbine had significantly different effects on the colon’s tonic response after hyperventilation ($P = 0.01$, adjusted for 5 tests).

**DISCUSSION**

Our results demonstrate that adrenergic modulation has different effects on the colonic tonic response during, as opposed to after, hyperventilation. Specifically, the $\alpha_2$-antagonist yohimbine attenuates the colonic tonic response after hyperventilation, but the adrenergic agents tested do not alter the colon’s tonic response during hyperventilation compared with placebo. Both frequency peaks of the heart rate spectral response decline during, but increase after, hyperventilation, lending support to the hypothesis that different autonomic mechanisms may be stimulated during the time when colonic tone is increased during and after hyperventilation.

The effects of hypocapnic hyperventilation represent central and peripheral effects of hypocapnia, as well as reflex responses resulting from baroreceptor, chemoreceptor, and lung stretch receptor stimulation (5, 8, 23). During hyperventilation, increased respiratory frequency and hypocapnia result in reduced parasympathetic input to the heart and a decrease in the RF max in R-R intervals. These findings are consistent with previous observations demonstrating an inverse relationship between the respiratory rate and the power of the RF component in R-R intervals (19). Conversely, in the 5-min epoch after hyperventilation, which was accompanied by bradycardia, vagal tone increased as manifested by a tendency toward increased power of the RF max in R-R intervals.

The non-RF max in R-R intervals are primarily responsive to variations in sympathetic tone but also respond to alterations in vagal tone. The reduced non-RF max peak during hyperventilation probably represents a reduction in sympathetic tone, consistent with other observations demonstrating a reduction in sympathetic neural traffic to skeletal muscle during hyperventilation in healthy volunteers (6). Similarly, the known physiological responses to hyperventilation tend to reduce sympathetic tone during, and increase sympathetic tone after, hyperventilation (6, 7, 23).

The spectral analysis data suggest a reduction in sympathetic and parasympathetic tone during hyperventilation. A reduction in vagal tone would be anticipated to reduce and not increase colonic tone. Clonidine and yohimbine, which are known to decrease and increase sympathetic tone, respectively, at the dose we employed, altered fasting colonic tone and produced significant hemodynamic effects but did not alter the colon’s tonic response during hyperventilation (10). Therefore, although the reduced inhibitory sympathetic input to the colon may contribute to the increase in colonic tone during hyperventilation, we suspect that direct effects of hyperventilation on smooth muscle predominate because the adrenergic agents had no effect on the colonic tonic response during hyperventilation. Hypocapnia has been shown to enhance tone via a peripheral effect in bronchial smooth muscle (20) and rabbit colonic taenia smooth muscle (14).

After hyperventilation, vagal and sympathetic tone increase, partly because of the central and peripheral effects of the dramatic reduction in respiratory rate, which alters the firing of pulmonary afferents (5). In addition, a component of stress, which is known to accompany hyperventilation, may contribute to the increase in colonic tone. Conceivably the $\alpha_2$-antagonist yohimbine reduces the colonic response after hyperventilation by increasing sympathetic traffic to the colon. Supporting this interpretation is the tendency of the $\alpha_2$-agonist clonidine to have the opposite effect, i.e., to increase the colonic tonic response after hyperventilation. An alternative explanation is that yohimbine attenuates the colon’s tonic response after hyperventilation by inhibiting vagal input to the colon, analogous to its ability to inhibit vagal outflow in animals (11, 13). This explanation is less plausible because phenylephrine did not influence the colonic tonic response after hyperventilation despite increasing vagal tone.

The heart rate spectral components may not be perfect surrogates for abdominal sympathetic and parasympathetic tone, consistent with the hypothesis of Janig and McLachlan (12) that the activities and sensitivities of sympathetic neurons subserving different functions, such as vasomotor and gastrointestinal motor functions, are under independent central control. It is conceivable that these different centers may have different propensities for respiratory modulation. Indeed, it has been suggested that respiration does not influence the activity of most neurons regulating pelvic organs in the cat (4, 12).

In summary, our studies suggest that different mechanisms are responsible for the enhanced colonic tone observed during, as opposed to after, hyperventilation. Our present results confirm previous findings that did not support a role for altered neural input in the tonic motor response during hyperventilation. In contrast, the increase in colonic tone after hyperventilation can be modulated by $\alpha_2$-adrenergic agents. Finally, these studies illustrate the complexity of autonomic modulation of the human colon’s motor function during a physiological reflex.

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MECHANISMS OF COLONIC EFFECTS OF HYPERVENTILATION

REFERENCES


