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Increased Colonic Motility During Exposure to a Stressful Situation

F. NARDUCCI, W. J. SNAPE, JR, W. M. BATTLE, R. L. LONDON, and S. COHEN

Colonic smooth muscle spike potentials and contractility were recorded during the periods of stress by a bipolar electrode-perfused catheter apparatus placed in the rectosigmoid colon. Healthy subjects and patients with the irritable colon syndrome (ICS) were exposed to three standardized stressful conditions: (1) ice-water immersion, (2) Stroop stimulus differentiation test, and (3) ball sorting. In healthy controls, colonic motility increased after the first exposure to ice-water immersion ($P < 0.05$), Stroop test ($P < 0.05$), or ball sorting. Respiratory frequency also increased after exposure to the stressful stimuli. However, repeat exposures to the stress tests did not stimulate colonic motility. An increase in colonic motility occurred in patients with the irritable colon syndrome pretreated with a placebo after exposure to ice water ($P < 0.05$), Stroop Test, or ball sorting ($P < 0.05$). However, after exposure to the stressful situations patients pretreated with chlordiazepoxide had a diminished increase in colonic motility or in respiratory frequency. These studies suggest: (1) in healthy controls habituation reduces the stress-related increase in colonic motility, and (2) in patients with the irritable colon syndrome, chlordiazepoxide decreases the stress-related increase in colonic motility.

During periods of emotional stress, abdominal pain increases and bowel function becomes irregular in patients with the irritable colon syndrome (ICS) (1–3). Symptoms often improve as the anxiety decreases (4, 5). Healthy subjects also may have disordered bowel function and colonic motility during periods of emotional stress (6–9).

This study evaluates: (1) the effect of an acute stress on colonic myoelectrical activity in healthy subjects and in patients with the irritable colon syndrome; and (2) the effect of lowering the reaction to stress by means of either pharmacological treatment (chlordiazepoxide) or habituation (10–12).

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From the Department of Medicine, Hospital of the University of Pennsylvania and Harbor-UCLA Medical Center.

Address for reprint requests: Dr. William J. Snape, Jr., Harbor-UCLA Medical Center, 1000 West Carson Street, Torrance, California 90509.

MATERIALS AND METHODS

Studies were performed on six healthy volunteers, 19–45 years of age, and 11 ICS patients, 19–42 years of age. Healthy subjects had no history of gastrointestinal disease or previous major abdominal surgery. The study was approved by the Committee on Human Experimentation of the University of Pennsylvania.

The ICS patients had abdominal pain related or unrelated to meals and an alteration of their bowel habits consisting of constipation or diarrhea for at least three months. Each patient had a negative sigmoidoscopy and barium enema within six months. Stool examination for ova, parasites, pathogenic bacteria, or blood was negative in each subject or patient. No patient or subject had a history of gastrointestinal disease other than the irritable colon syndrome.

Five healthy volunteers were studied three times, 5–14 days apart; one volunteer had only the first study. In the first study the six healthy subjects received a placebo tablet 30 min prior to the study in a single-blind manner; the second and third studies were administered in a double-blind crossover manner, comparing chlordiazepoxide (10 mg) to an identical-looking placebo. Each ICS patient was studied only once, in a double-blind (noncrossover) manner. Each patient received either chlordiazepoxide (10 mg) or placebo.

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Each patient or healthy subject underwent a sigmoidoscopy without air insufflation after at least 8 hr of fasting. Two bipolar silver–silver chloride wire electrodes were attached to the colonic mucosa, through the sigmoidoscope (13). Each bipolar electrode was connected to a rectilinear recorder (Beckman, R 611) and an analog magnetic tape recorder. The amplified signal was passed through a 0.16-Hz high-pass filter and a 30-Hz low-pass filter before analysis. All subjects were grounded through a surface electrode attached to the right leg. Intraluminal pressure was measured at the same level as each recording electrode, by constantly perfused catheters, using a low-compliance infusion pump (Arndorfer Medical Specialties). Pressure was transmitted through transducers (Statham, 231A) to the recording devices. Respirations were monitored by a pneumograph belt placed around the chest.

After the insertion of the electrode and the intraluminal pressure catheter, the patient ingested two coded capsules containing either placebo or chlordiazepoxide (10 mg) (Hoffman-LaRoche Laboratories). After an adaptation period of 60 min, myoelectrical and motor activity were recorded during a baseline of 30 min. Each subject or patient was subjected to the stressful stimuli.

The following acute stress stimuli were applied:

Cold Pressor Test. One hand was immersed in ice-cold water (+4° C) for 3–5 min.

Stroop Test. Subjects were exposed to two overlapping, but different stimuli that the subject had to separate and appreciate in a previously determined sequence (14). Subjects must read in fast sequence 50 cards on which the names of a color (green, etc) is written in another color (blue, etc). The subject was exposed to each card for 2 sec in fast sequence.

Ball Sorting. By trial and error the subject was required, within a certain time period, to fit small balls (⅛–¼ in.) which have slight variations in diameter into holes of the same diameters.

Myoelectrical activity was evaluated for each 15-min period. Spike potentials were counted with a digital electronic counter and confirmed by visual analysis (15). The intraluminal pressure activity was evaluated by determining an estimated motility index (ie, product of the mean amplitude of the pressure waves multiplied by the sum of duration of each pressure wave) (13). This method correlates with the exact area under the curve of each pressure wave calculated by a computer program. The contraction frequency was determined from each series of contractions present continuously for at least 60 sec. Respiratory frequency was determined by averaging the three randomly chosen 60-sec blocks for each 15-min period. All recordings were interpreted by an investigator who was unaware of the treatment administered.

Data were evaluated statistically using paired and unpaired Student's t test.

RESULTS

Figure 1 shows the number of spike potentials (SP) recorded from the colon in normal subjects during the control period and each of the three 15-min periods of stress. During the first study, each subject received a placebo. During the control period, before the stimuli, 3.3 ± 1.4 SP/15 min occurred. Ice-water immersion (9.8 ± 2.0 SP/15 Min) ($P < 0.02$) or the Stroop test (13.2 ± 4.2 SP/15) ($P < 0.05$) increased colonic spike potentials. Ball sorting also increased colonic spike activity (10.0 ± 3.8 SP/15 min), but not significantly ($P > 0.05$).

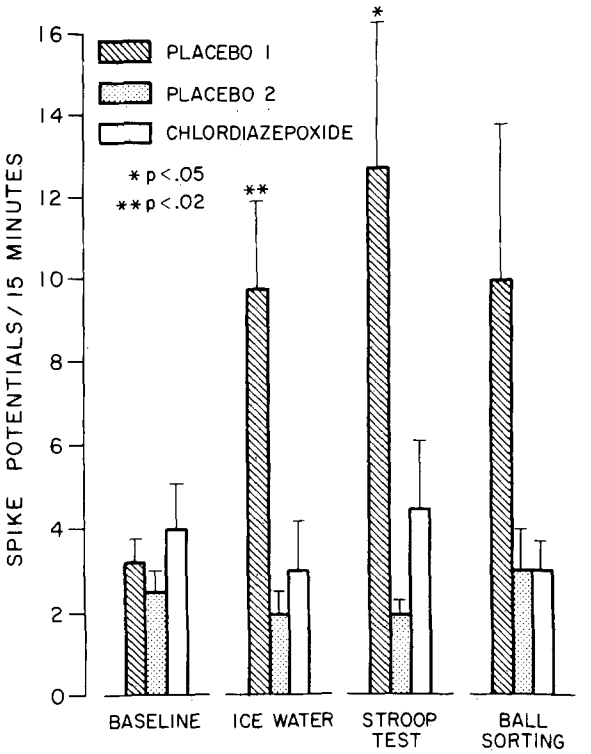

Fig 1. Effect of acute stress on colonic spike activity in healthy subjects. The response to the acute stresses of ice water, Stroop test, and ball sorting are compared to the baseline. The effects of pretreatment with placebo (first study) and placebo and chlordiazepoxide (repeat studies) are shown. Each value is the mean + SEM for at least five subjects.

There was little variation of baseline spike potentials during the three studies ($P > 0.05$). However, during the repeat studies, there was no stress-induced increase in spike potentials above baseline after premedication with placebo or chlordiazepoxide ($P > 0.05$). Spike potentials after taking either the second placebo or chlordiazepoxide were significantly less after ice-water immersion and the Stroop test ($P < 0.05$), than during the first exposure to stress. The colonic response to ball sorting was also decreased.

Colonic contractility increased concomitantly with the increase in colonic spike activity (Table 1).

TABLE 1. MOTILITY INDEX* BEFORE AND AFTER STRESS TESTS

	Basal	*Ice water*	*Stroop*	*Ball sorting*
Normal (placebo)	50 ± 12	722 ± 308†	1530 ± 211‡	820 ± 403
IBS (placebo)	47 ± 28	1283 ± 765	1840 ± 150†	1629 ± 923
IBS (chlordiazepoxide)	268 ± 93	467 ± 212	676 ± 209	1177 ± 464

*All values expressed as mm^2/15 min.
†$P < 0.05$.
‡$P < 0.01$.

Contractile activity at 3 cycles/min was present 9.0 ± 6.4% of the recording time after stress only. The motility index during the control period was 50 ± 12 mm^2/15 min. During the first exposure to the stress tests, the motility index increased after the Stroop test (1530 ± 211 mm^2/15 min) ($P < 0.01$) and ice-water immersion (722 ± 308 mm^2/15 min) ($P < 0.05$). Ball sorting increased the motility index (820 ± 403 mm^2/15 min), but did not reach significance ($P > 0.05$). However, during the second and third exposures to the acute stress, no increase in the colonic motility index occurred after any of the stimuli.

The respiratory rate was measured as an independent measure of the subjects reaction to this stressful stimuli. Figure 2 shows the respiratory rate before and after the stressful stimuli in healthy subjects. During the initial exposure to each stress test, respiratory frequency increased over baseline ($P < 0.05$). Respiratory frequency during the second or third exposure to stress was lower than during the first exposure ($P < 0.05$). Thus, an habituation to the stress occurred in the subjects after the first study for both the respiratory frequency and the colonic motility response.

To eliminate habituation, we modified the experimental design for ICS patients. The patients were administered chlordiazepoxide or placebo in a double-blind noncrossover manner.

Figure 3 shows the number of spike potentials/15 min in patients with ICS patients pretreated with placebo. The number of spike potentials during the control period (3.6 ± 1.7 SP/15 min) was similar to healthy controls ($P > 0.05$). Colonic spike activity increased after ice water (8.3 ± 3.3 SP/15 min) ($P <$

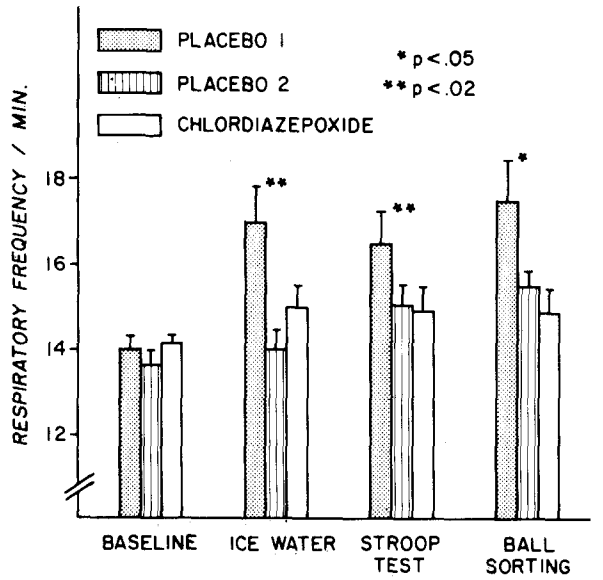

Fig 2. Effect of acute stress on respiratory frequency in healthy subjects. The response to stress is compared to baseline. Each value is the mean + SEM for at least five subjects.

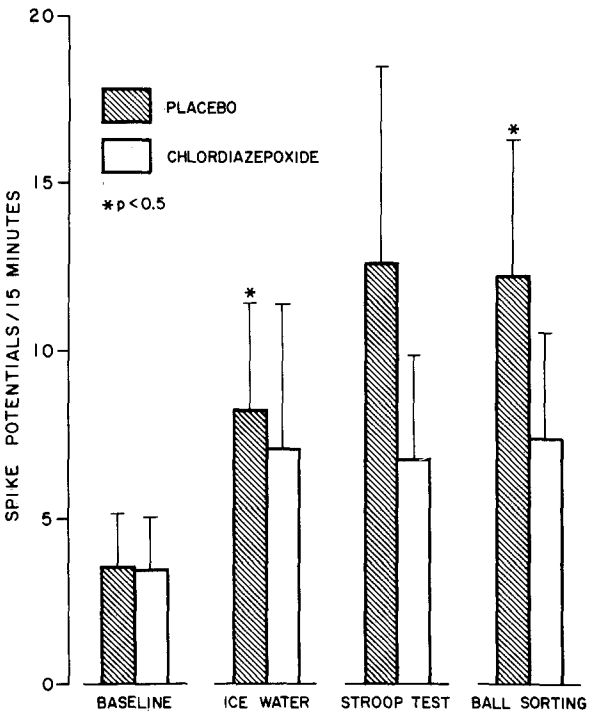

Fig 3. Effect of acute stress on colonic spike activity in patients with the irritable colon syndrome. The response to acute stress is compared to baseline for placebo and chlordiazepoxide pretreatment. Each value is mean + SEM for at least five subjects.

0.05), the Stroop test (12.8 ± 6.0 SP/15 min), or ball sorting (12.0 ± 4.3 SP/15 min) ($P < 0.05$). This increase in spike activity was reproducible in all patients. In contrast, if the patients took chlordiazepoxide (10 mg), the spike activity associated with the stress tests was decreased.

The motility index in patients with the irritable colon syndrome increased after the stressful stimuli (Table 1). Contractions, at 3 cycles/min, were present 20.8 ± 7.6% of the recording time after stress. The motility index during the control period in patients with ICS (47 ± 28 mm^2/15 min) was similar to healthy controls ($P > 0.05$). The greatest increase in the motility index occurred after the Stroop test (1840 ± 150 mm^2/15 min) ($P < 0.05$). The motility index increased after ice water (1283 ± 765) and ball sorting (1629 ± 923), but did not reach significance. As in the healthy subjects, a slight increase of respiratory frequency was noted during stress tests after the placebo, (21.6 ± 1.5/min) compared to baseline (18.4 ± 1.3/min).

The increase in colonic contractile activity was insignificant in patients treated with chlordiazepoxide. Also, there was no increase in the respiratory frequency during the stress periods, if the patients were pretreated with chlordiazepoxide ($P > 0.05$).

DISCUSSION

This study shows that standardized acute stressful situations stimulate colonic motility both in normal subjects and in patients with irritable colon syndrome. The increase in colonic motor function corresponded to a parallel increase in respiratory frequency, an index of the general response to the stress.

The mechanism through which stress induces the observed increase in colonic myoelectric and motor activity is unknown, but different pathways may be involved. First, electrical stimulation of certain areas of the central nervous system increases colonic motility (16). These exictatory impulses are transmitted to the colon through both the sympathetic lumbar colonic nerves and the parasympathetic pelvic nerves. Second, after stressful stimuli, the increase in circulating catecholamines (17) may stimulate colonic motility (18). While high concentrations of norepinephrine inhibit colonic motor activity, low concentrations of noreinephrine and epinephrine stimulate myoelectrical activity of cat colon *in vitro* (18) and increase the amplitude of contractions of cat colonic circular, but not longitudinal, muscle strips (19). Third, endogenous opiates are released after stress (20). Opiates stimulate colonic motor activity (21–23), and may mediate the increase of colonic motor activity observed in humans after eating (24).

When colonic contractility is increased in patients with ICS, the contractions often have a frequency of 3 cycles/min (25, 26). These contractions are nonpropulsive and may be manifestations of segmental or haustral activity (13). An increase in segmental contractile activity during a stressful situation may explain the exacerbation of symptoms that may occur in ICS (1–4).

When stressful stimuli were repeated in healthy subjects, colonic spike activity did not increase. Thus, it appeared that the subjects had habituated to the stressful stimuli and were no longer distressed by the stimuli (10–12). This explanation is supported by the corresponding lack of increase in respiratory frequency during the repeat studies. The effect of adaptation to stress on gastrointestinal motility recently has been reported, and relaxation training has been proposed in the treatment of patients with ICS (27). We did not test for adaptation in the patients with ICS. However, other studies showed that patients with ICS have difficulty adapting to life events and social relationships, and they may be less likely to spontaneously habituate (3).

To eliminate the effects of habituation in patients with ICS, the effects of chlordiazepoxide or placebo on stress-stimulated colonic motility were evaluated by a double-blind noncrossover study. Chlordiazepoxide decreased the effect of stress on colonic motor function in ICS patients. Chlordiazepoxide is a benzodiazepine with central nervous system activity and also peripheral smooth muscle-relaxant properties (28). Both these actions may contribute to the beneficial effect of chlordiazepoxide on the increased colonic motor function induced by stress.

In conclusion, acute stress increases colonic motor activity both in healthy subjects and in ICS patients. Habituation in normal subjects and chlordiazepoxide in ICS patients prevented the stress-induced increase of colonic motor activity.

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