Colorectal responses to distension and feeding in patients with spinal cord injury

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Sutter VP, Ng C, Rutkowski S, Hansen RD, Kellow JE, Malcolm A. Colorectal responses to distension and feeding in patients with spinal cord injury. Am J Physiol Gastrointest Liver Physiol 296: G1344–G1349, 2009. First published April 9, 2009; doi:10.1152/ajpgi.90408.2008.—The role of the central nervous system (CNS) in the normal gastrocolonic response is controversial. Our aims were as follows: 1) to evaluate colorectal, rectocolic, gastrocolonic, and gastrorectal reflex responses in patients with cervical spinal cord injury (SCI) and 2) to compare these responses with those in healthy subjects. In six patients with SCI (5 male, 42 ± 4 yr) and six healthy control subjects (5 male, 36 ± 5 yr), 2-min phasic distensions were performed randomly via dual-barostat balloons in the colon and rectum. Continuous colonic and rectal balloon volumes were recorded during distensions and after a 1,000-kcal liquid meal. Mean balloon volumes were recorded before, during, and after phasic distensions and over 60 min postprandially. The colorectal response was similar in control subjects and SCI patients (rectal volume reduction = 28 ± 11% and 15 ± 5% in SCI patients and healthy subjects, respectively); the rectocolic response was variable. The gastrocolonic response was present in all subjects (colonic volume reduction = 49 ± 4% and 44 ± 3% in SCI patients and healthy subjects, respectively), with a time effect in the first 30 min (P < 0.0001) and a group effect in the second 30 min (P < 0.004). The gastrorectal response was present in four SCI patients and five healthy subjects (rectal volume reduction = 38 ± 4% and 41 ± 3% in SCI patients and healthy subjects, respectively), with a time effect in the first 30 min (P < 0.0001) but no group effect in the second 30 min. Intact neural transmission between the spinal cord and higher centers is not essential for normal colorectal motor responses to feeding and distension; however, a degree of central nervous system and neurohormonal modulation of these responses is likely.

gastrocolonic; gastrorectal; rectocolic; colon; spinal injury

The study of reflex motor activity within the gut has received increasing attention in recent years. In reference to the colorectum, previous studies demonstrated that distension of the descending colon can be associated with an increase in rectal tone, a phenomenon termed the “colorectal” reflex (14, 20). In addition, rectal distension provokes an opposite effect, with a reduction in colonic tone and phasic motor activity, a phenomenon termed the “rectocolic” reflex. In healthy subjects, Law et al. (14) found that the rectocolic response was clear and reproducible but the colorectal response was more subtle; conversely, studies from our unit demonstrated a clear and definitive colorectal response and a more variable rectocolic response (20).

The neural pathways involved in these reflexes in humans, particularly the roles of intrinsic vs. extrinsic pathways and the role of the spinal cord, remain unclear. Patients with complete spinal cord injury (SCI) provide a unique human model to delineate these neural pathways, inasmuch as spinal pathways are severed, yet local intrinsic pathways are preserved. The study of enteric motor reflexes in patients with SCI is clinically important, because such patients suffer from significant bowel dysfunction (21) and have repeatedly rated their bowel dysfunction as a moderate-to-severe life problem, second only to loss of mobility (11, 15).

The intestinal motor response to meal ingestion has received considerable attention and is a well-substantiated, reproducible response. Nevertheless, the neural mechanisms involved are not clearly understood in humans, and controversy remains. Thus manometric studies in healthy subjects showed a colonic meal response after sham feeding (23), indicating a cephalic or central nervous system (CNS) response. On the other hand, an early study in one patient with lumbar SCI (6) also found a colonic manometric response to the sight of food, and in myoelectric studies in healthy subjects, Sun et al. (26) failed to demonstrate a gastrocolonic response to sham feeding, suggesting a lack of CNS involvement in the response. In terms of the colonic motor response to meal ingestion, Bruninga et al. (4), in a single SCI patient, reported an impaired colonic tonic response, a finding that again supported the participation of the CNS in the normal gastrocolonic response. In contrast, Connell et al. (6) demonstrated a definite colonic manometric response to a meal in two cervical SCI patients, indicating the presence of this response without CNS input. In contrast to the gastrocolonic response, the gastrorectal response has received relatively little attention; in one study, this response was found in two-thirds of healthy subjects (24). In myoelectric studies in SCI subjects, Aaronson et al. (1) failed to demonstrate a normal gastrorectal response to a meal, a finding again supportive of CNS involvement in such enteric reflexes.

Because of the controversy regarding the neural pathways mediating these motor responses, we undertook a detailed study of both of these aspects in patients with SCI. Our hypotheses were as follows: 1) gastrocolonic and gastrorectal tonic responses would be present in cervical SCI patients, although the reflexes would be altered because of involvement of cervical spinal transmission, and 2) colorectal and rectocolic tonic responses would be preserved in cervical SCI patients, inasmuch as these reflexes are likely to depend on local regional neural pathways. Our aims, in patients with cervical SCI, were as follows: 1) to evaluate the colorectal and rectocolic tonic responses in the fasting state and 2) to evaluate the gastrocolonic and gastrorectal tonic responses to a standard meal. We also compared these responses with those in healthy subjects. Dual-barostat technology enabled us to examine colonic and rectal tonic responses to distension and, concurrently,
the colonic and rectal tonic responses to feeding. Before this study, there have only been case reports of colonic barostat studies in SCI patients, and no studies in SCI patients have incorporated dual-barostat technology in a comprehensive assessment of both types of reflexes in one patient.

METHODS

Subjects

Six patients (5 male, 42 ± 4 yr old) with established SCI were recruited from the Spinal Injuries Unit at Royal North Shore Hospital. All patients had complete C4–C7 spinal cord lesions [as determined by motor and sensory examination (7)] of ≥12-mo duration. All SCI patients underwent standard anorectal manometry, as described elsewhere (22), which revealed low resting anal sphincter pressure (39 ± 9 mmHg) and low squeeze anal pressure (43 ± 9 mmHg), as well as inadequate rectal pressure with strain and often absent anal relaxation with strain. Six asymptomatic healthy-age-matched individuals (5 male, 36 ± 5 yr of age) comprised the control group. Exclusion criteria were significant autonomic dysreflexia, significant pressure ulceration, previous gastrointestinal surgery, concurrent significant medical conditions, and pregnancy. Subjects of child-bearing capability recorded a negative urine human chorionic gonadotrophin pregnancy test.

All SCI patients were routinely managed in the community with a stable bowel care regimen of assisted evacuation, and all completed the Rome II integrative symptom questionnaire (8). No SCI patient reported bloating or fullness after eating, or diarrhea. Although one SCI patient reported constipation (<3 bowel actions per week), all patients relied on a routine of regular bowel evacuation. The study was approved by the Human Research Ethics Committee of the Royal North Shore Hospital. Written informed consent was obtained from all subjects before commencement of the study.

Experimental Protocol

In each subject, a dual-barostat assembly (Distender Series II, G & J Electronics, Toronto, ON, Canada) was positioned, as previously described (19), using left-sided colonoscopy without sedation after colonic lavage with 4 liters of polyethylene glycol solution (Cololytely, Dendy Pharmaceuticals, Brighten, Victoria, Australia). Polyethylene balloons (Hefty Baggies, Mobil Chemical, Pittsford, NY), with infinite compliance and a maximum volume of 600 ml, were tied at both ends to the barostat catheter and placed in the descending colon and in the rectum; their positions were confirmed by fluoroscopy.

A conditioning distension followed by determination of the individual operating pressure (IOP), taken as the value 2 mmHg above the pressure at which respiratory variation was observed, was undertaken in each subject. A slow ramp distension (2 mmHg/30 s) in the colon and rectum to a pressure of 40 mmHg was carried out to obtain compliance data. A 5-min rest period was then allowed to enable balloon volumes to reach each individual’s baseline. For evaluation of the colorectal and rectocolic responses, phasic distensions of 20 mmHg above IOP and 2-min duration were performed in the colon and rectum in each subject, while the volume in the opposing balloon was recorded (2, 20). All subjects recorded the sensation of gas, urge, and pain in response to the phasic distensions on a 10-cm visual analog scale, with a score of 0 for no sensation and 10 for maximal sensation. Thereafter, for evaluation of the colonic and rectal response to feeding, colonic and rectal balloon volumes were continuously recorded for 60 min following the ingestion of a standard 1,000-kcal (53% fat, 35% carbohydrate, 12% protein) liquid meal. The recordings were then ceased, and the barostat-catheter assembly was removed.

Data and Statistical Analysis

The colorectal reflex was defined as the alteration in rectal tone, as measured by a change in the rectal balloon volume, in response to the colonic phasic distension. The mean volume in the rectal balloon was measured over 2-min periods before, during, and after the colonic distension (20). Similarly, the rectocolic reflex was defined as the alteration in colonic tone, as measured by a change in the colonic balloon volume, in response to the rectal phasic distension (20). All data were checked for normality of distribution using Kolmogorov-Smirnov tests. Appropriate parametric (for normally distributed data) and nonparametric (for nonnormally distributed data) tests were then applied. All data were normally distributed, except where indicated. Repeated-measures ANOVA was used to determine significant time (before, during, and after distension) and group (SCI patients vs. healthy subjects) effects. Student’s paired and independent t-tests and Wilcoxon signed-rank tests and Mann-Whitney U-tests were used to further assess responses to distension in SCI patients and healthy subjects.

The gastrocolonic and gastrectocolic reflexes were defined as the colonic and rectal tonic responses, measured by the change in the respective barostat balloon volumes, after the meal (24). The mean volumes in the balloons were measured during a baseline period of 10 min before the meal and again at 5-min intervals postprandially for 60 min. Repeated-measures ANOVA was used to determine significant effects of time and group for two 30-min epochs postprandially. Analyses were undertaken with SPSS version 11.0 (SPSS, Chicago, IL), with the level of significance set at P < 0.05. Values are means ± SE.

RESULTS

Colonic and Rectal Tonic Responses to Distension

Rectal tonic response to colonic distension (colorectal reflex). Figure 1 shows the rectal response to colonic distension in a representative healthy subject and a representative SCI patient. The colorectal reflex was present in all healthy subjects and all SCI patients. Figure 2A shows the average rectal volumes for both groups before, during, and after colonic distension. Although ANOVA did not reveal a significant time effect or a group-time interaction, there was a trend (P = 0.06) for a group effect. When predistension vs. distension data were compared (Fig. 2B), rectal volume decreased with distension in healthy subjects (P = 0.03, by paired t-test) and SCI patients (P = 0.03, by Wilcoxon signed-rank test, marginally nonnormally distributed data). The mean reduction in rectal balloon volume in SCI patients was 28 ± 11%, which was not significantly different from that in healthy subjects (15 ± 5%). In healthy subjects and SCI patients, the mean postdistension value did not differ statistically from the mean predistension value.

Colonic tonic response to rectal distension (rectocolic reflex). The rectocolic reflex (increase in colonic volume in response to rectal distension) was present in only one SCI patient (30% volume increase) and two healthy subjects (25% and 15% increase). In one SCI patient and one healthy subject, there was no significant alteration in colonic volume, whereas in four SCI patients and three healthy subjects, colonic volume was decreased (61% in SCI patients and 21% in healthy subjects) in response to rectal distension. Figure 3A shows the average colonic volumes of both groups before, during, and after rectal distension. Individual predistension and distension data are shown in Fig. 3B. No significant group or time differences or group-time interaction was demonstrated.
Colonic and Rectal Tonic Responses to Meal Ingestion

Colonic tonic response to meal ingestion (gastrocolonic reflex). The gastrocolonic reflex was present in all healthy subjects and SCI patients. The mean decrease in colonic volume over 60 min postprandially was similar in SCI patients and healthy subjects (49 ± 4% and 44 ± 3%, respectively). In both groups, colonic volume decreased during the first 30-min epoch. In healthy subjects, the maximal response occurred at 20 min after meal ingestion; in SCI patients, however, there was a more sustained decrease in colonic volume, with a maximal response at 45 min. Thus there was a significant effect of time in the first 30-min epoch (P < 0.0001) and a significant difference between groups in the last 30-min epoch (P < 0.004; Fig. 4).

Rectal tonic response to meal ingestion (gastrorectal reflex). The gastrorectal reflex was present in four SCI patients and five healthy subjects (38 ± 4% and 41 ± 3% decrease in rectal volume over 60 min postprandially in SCI patients and healthy subjects, respectively). There was a significant effect of time in the first 30-min epoch (P < 0.0001), with no difference between groups in the second 30-min epoch. There was a maximal response in both groups at 25 min after meal ingestion (Fig. 5).

Colonic and Rectal Baseline Parameters

There was no significant difference (by t-test) in the rectal IOP between SCI patients and healthy subjects (10.3 ± 0.8 and 9.0 ± 0.4 mmHg, respectively). The colonic IOP, however, was lower in SCI patients than in healthy subjects (10.3 ± 1.0 vs. 15.7 ± 0.3 mmHg, P = 0.003, by Mann-Whitney U-test, nonnormally distributed data). There was no significant difference (by t-test) in the colonic (133 ± 45 and 83 ± 12 ml in SCI patients and healthy subjects, respectively) or rectal (58 ± 12 and 92 ± 25 ml in SCI patients and healthy subjects, respectively) balloon volumes at baseline between groups. Perception data of control subjects included mean visual analog scale values for gas, urge, and pain of 0.8 ± 0.5, 1.6 ± 0.7, and 0.1 ± 0.1 cm for colonic distension and 0.5 ± 0.3, 5.8 ± 1.1, and 0.1 ± 0.1 cm for rectal distension. There was no difference in colonic or rectal compliance between groups (7.0 ± 2.1 and 10.5 ± 2.0 mmHg/ml, respectively, in SCI patients and 5.2 ± 0.4 and 7.4 ± 0.8 mmHg/ml, respectively, in healthy subjects), and premeal baseline volumes were similar in SCI patients (131 ± 19 and 119 ± 37 ml for colonic and rectal, respectively) and healthy subjects (100 ± 12 and 78 ± 27 ml for colonic and rectal, respectively).

DISCUSSION

Our experiments represent the first report of the use of dual-barostat technology in patients with SCI. These studies are technically demanding, even in healthy subjects, and especially in patients with such limited mobility. The novel findings are the preservation of the colonic and rectal tonic responses to feeding and the colorectal reflex in cervical SCI patients compared with healthy subjects. Our findings support both of our hypotheses, with the proviso that the rectocolic tonic response was variably present in both groups.

Preservation of the colorectal reflex in SCI patients suggests that this type of tonic activity does not depend on neural transmission through central spinal pathways. Innervation of the distal colon and rectum arises from spinal cord segments S2–S4 for the parasympathetic fibers and from the lumbar spinal column for the sympathetic fiber (16), and extrinsic neural pathways have been deemed generally necessary for colonic motility (13). Our study, however, suggests that local neural pathways may be important. We acknowledge that our study comprised small subject numbers, raising the possibility of type II error in the comparison of responses in healthy
The gastrocolonic response in cervical SCI patients was clearly demonstrated in our study. Bruninga et al. (4), in a single SCI patient, found that the gastrocolonic tonic response was absent but meal-induced phasic contractile activity was preserved. Connell et al. (6), in two cervical SCI patients, showed an increase in sigmoid motor activity with a meal, similar to that in healthy subjects. In addition, using anorectal manometry, Walter et al. (29) showed a postprandial increase in rectal pressure in patients with SCI. In contrast, Glick et al. (10) failed to demonstrate a gastrocolonic response in nine patients with SCI; however, they studied a lower level of injury. Aaronson et al. (1), using myoelectric evaluation in three cervical SCI patients, also failed to demonstrate a meal response, although they evaluated only the gastrorectal response, and a higher level of basal rectal activity was noted. Our study did confirm the presence of a gastrorectal response,

Fig. 2. Colorectal reflex. A: no significant time (predistension, during a 2-min colonic distension, and after distension) effect, but a trend for a group effect (SCI patients vs. healthy subjects, $P = 0.06$) on mean rectal balloon volume was found when the 3 time points were compared. B: when predistension vs. distension values only were compared (individual values), a significant reduction in rectal volume during colonic distension was found in SCI patients ($P = 0.03$) and healthy subjects ($P = 0.03$).

Fig. 3. Rectocolic reflex. A: no significant group (SCI patients vs. healthy subjects) or time (predistension, during a 2-min rectal distension, and after distension) effects on mean colonic balloon volume was found when the 3 time points were compared. B: when predistension vs. distension values only were compared (individual values), no significant change in colonic volume during rectal distension was found in SCI patients or healthy subjects.
in addition to the gastrocolonic response, with use of our dual-barostat technique. Dual-barostat technology enables improved evaluation of enteric reflexes, inasmuch as it is not influenced by basal enteric activity, and it provides sensitive assessment of the tonic activity of large-diameter organs, such as the colon and rectum. With respect to baseline motor function, the colonic IOP was lower in SCI patients than in healthy subjects. Baseline differences have also been demonstrated in prior myoelectric and manometric studies (1, 6). By setting operating pressures in individual subjects at the commencement of each study, we could reliably compare responses in healthy subjects and SCI patients.

Preservation of the colonic tonic response to a meal in SCI patients supports the notion that the meal response does not depend entirely, or even significantly, on central pathways. Other possible mechanisms that need to be considered include intrinsic neural pathways, as suggested by Connell et al. (6); short neural pathways via prevertebral ganglia, as suggested by Kreulen and Szurszewski (12) from guinea pig studies; and vagal pathways, a notion supported by Snape et al. (25), who showed inhibition of the meal response after anticholinergic administration; as well as by Cao et al. (5), in a recent rat study of central vagal stimulation. Additional factors could include serotonergic pathways (3) or humoral pathways that remain to be elucidated (4).

The gastrocolonic response is known to comprise a mechanoreceptor-derived component stimulated by gastric antral distension and a chemoreceptor component activated by nutrient delivery (3). We noted differences in the timing of the early and late phases (which may correspond to the neural and hormonal response phases, respectively) of the gastrocolonic reflex, with the later phase of the gastrocolonic reflex being more prominent in SCI. One possible explanation for this a greater dependence of the gastrocolonic response on upregulated hormonal influences, rather than neural factors, in SCI patients than in healthy subjects. Another possible explanation is loss of, or other alteration in, the normal CNS modulation in SCI patients. We believe that the difference in the later phase of the gastrocolonic response is unlikely to be due to gastroparesis in SCI patients (9), inasmuch as there was no delay in the gastrorectal reflex measured simultaneously.

Our data suggest that since colorectal reflex activity is relatively preserved, chronic constipation in these patients may be at least partly attributable to anorectal dysfunction after SCI, as has been described previously (17, 27). Recently, Lynch et al. (18) proposed that patients with upper motor neuron lesions could potentially use digitation to facilitate defecation. Our findings provide physiological evidence for the clinical recommendation that such maneuvers may be more effective after meal intake.

In conclusion, our finding of the preservation of the gastrocolonic response in cervical SCI is the most definitive demonstration of this to date. In addition, the colorectal response has not previously been investigated in such patients. Our demonstration of the presence of both of these reflexes provides unique insight into the pathways involved. Both of these results indicate that these reflexes do not depend on transmission through the cervical spinal cord. These reflexes therefore may be transmitted via intrinsic nerves or prevertebral pathways.

Fig. 4. Gastrocolonic reflex, or colonic motor response to meal ingestion, as measured by a progressive increase in colonic tone (decrease in colonic volume) postprandially. Nadir (maximal response) occurred at 20 min in healthy control subjects and 45 min after meal ingestion (t0) in SCI patients. There was a significant effect of time in the first 30-min epoch (P < 0.0001) and a significant group effect in the second 30-min epoch (P < 0.004).

Fig. 5. Gastrorectal reflex is demonstrated as a progressive increase in rectal tone (decrease in rectal volume) after meal ingestion (t0). Nadir occurred at 25 min after meal ingestion (t0) in both groups, with a significant effect of time in the first 30-min epoch (P < 0.0001) and no group effect in the second 30-min epoch. NS, not significant.
(for the colorectal and rectocolic reflexes) and vagal and neurohormonal pathways (for the gastrocolonic reflex).

GRANTS

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