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BRIEF COMMUNICATION

Eating Lowers Defecation Threshold in Pigs Through Cholinergic Pathways

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CROWELL, M. D., F. MUSIAL AND A. W. FRENCH. *Eating lowers defecation threshold in pigs through cholinergic pathways.* PHYSIOL BEHAV **53**(5) 1029–1032, 1993.—The effect of atropine on defecation threshold was compared to placebo pre- and postprandially in four 20- to 30-kg pigs. Stepwise balloon distention was performed 10 cm from the anal verge with a 5-cm latex balloon. Volume was increased in steps of 10 ml up to 200 ml of air or until the balloon was defecated (defecation threshold). Dependent measures were balloon volume, rectal pressure, rectal compliance, and an index of distention-induced contractile activity. Under placebo conditions, the volume and pressure to elicit defecation were significantly lower after feeding ($p < 0.05$). The distention-induced contractile activity significantly increased near the defecation threshold, but pre- and postprandial conditions were not different. No differences were seen between pre- and postprandial rectal compliance curves. Atropine abolished the postprandial decrease in defecation threshold, but did not affect rectal compliance. The increase in contractile activity at defecation threshold seen with placebo was abolished by atropine. These results show that eating lowers the defecation threshold in terms of distention volume and rectal pressure, and demonstrate that these changes are mediated through cholinergic pathways.

Defecation threshold Pigs Rectal balloon distention Feeding Atropine

MANY patients suffering from gastrointestinal disorders experience bowel symptoms of pain, diarrhea, imperative urge to defecate, or fecal incontinence following food ingestion. Colonic myoelectric and contractile activity increases for up to 50 min after eating (12). The magnitude and duration of this effect, called the gastrocolonic response, depends on the caloric content and the composition of the meal (11). If it contains more than a minimal amount of fat, there may be a second delayed peak in colonic motility (12). The second peak is mediated by gastrointestinal hormones (10,12) and can be inhibited by amino acids (1,6).

Atropine, which blocks acetylcholine pathways through muscarinic receptors (8), has been shown to abolish the early increase in colonic motor activity associated with the gastrocolonic response (14). Furthermore, neostigmine, an acetylcholinesterase inhibitor, and therefore a smooth muscle stimulant, enhanced the neurally mediated part of the gastrocolonic response (14). These data suggest that acetylcholine pathways are involved in the mediation of the gastrocolonic response.

The gastrocolonic response may influence sensory thresholds as well as motor activity. Erckenbrecht et al. (4) reported that the volume required to induce an urge to defecate was reduced during and immediately following a meal, indicating a postprandial decrease in the threshold for colonic perception. However, measurement of perception thresholds in humans is problematic because the occurrence of the physiological signal is confounded with the decision of the individual to respond (5). This poses a particular problem for the measurement of defecation threshold compared to pain threshold, since the pain threshold is more distinct than the urge to defecate. Studying actual defecation rather than the self-reported urge to defecate would overcome many of these problems. However, measuring defecation in humans is difficult due to interactions with social and behavioral norms. Therefore, we attempted to overcome these methodological limitations by studying the actual defecatory response using a large animal model.

Initial results from our laboratory using pigs (7) supported the data of Erckenbrecht et al. (4). The threshold for balloon defecation was decreased postprandially in terms of distention volume and rectal pressures. This effect was not mediated through changes in rectal compliance or distention-induced contractile activity, and was thought to reflect a change in visceral perception resulting in volitional defecatory behavior.

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The aims of this study were to replicate earlier findings of eating-induced reductions in defecation threshold and to investigate the effect of atropine on this response.

METHOD

Apparatus

The recording system consisted of a commercially available pressure transducer catheter containing a silicon diffused, solid-state, pressure transducer catheter (model SSD-382, Millar Instruments, Houston, TX), a battery-operated, programmable data recorder (Omnidata PC 703, Orem, UT), and a distention balloon probe consisting of a rubber open-tip catheter (18 F) with a thin latex balloon (5 cm) tied airtight over the opening. The pressure transducer was placed inside the rubber catheter so that pressures in the balloon were conducted to the transducer and could be recorded.

Subjects

Three Yucatan Micropigs (Charles River Co., Wilmington, MA) and one domestic pig (all females between 20 and 30 kg) were used in this study. The animals were housed individually in accordance with the American Association for Accreditation of Laboratory Animal Care guidelines in an air- and light-controlled room. The animals were fed commercial pig chow (500 g) once a day.

Experimental Protocol

During rectal distention the pigs were comfortably restrained in a padded nylon sling. Trials were performed with one investigator inserting the rectal probe and handling the recording equipment, and a second person supporting the pigs' legs and calming them if necessary. No bowel preparation was used.

Two recording sessions were performed in each pig for each drug condition [atropine (0.05 mg/kg) vs. saline]. Drug conditions were counterbalanced. Drugs were administered intravenously as a bolus 20 min before the beginning of the first trial (8,14). Each session lasted approximately 90 min, including a feeding period of 10–15 min. Pigs were restrained during drug administration and rectal distention but not during feeding. Recording sessions were separated by 1 week.

The balloon probe was placed 10 cm from the anal verge. The probe was marked in cm and the position was monitored throughout the procedure. Rectal balloon distention was performed by adding 10 ml increments of air until the balloon was expelled or 200 ml of air was reached. The defecation threshold was defined as volume and pressure in the balloon at the time it was defecated. Pressures were sampled at 1 Hz and averages determined for every stimulation volume. Dependent measures were balloon volume and rectal pressure. Rectal compliance (calculated as the ratio of cumulative pressure changes to cumulative volume changes over all measurements) is a measure of active resistance to lumenal distention in the bowel and may play a role in rectal sensitivity.

Distention-induced contractile activity (motility index) was calculated for each distention volume. The contractile activity was calculated as the sum of the area under the curve per unit time (9). Mean values for the first 3-min interval of each trial were compared to the means of the final 3-min interval preceding defecation, as were pre- and postprandial predefecation intervals and drug conditions.

Data Analysis

Volume and pressure at defecation threshold were compared using a three-way repeated measures ANOVA. The factors were feeding condition (pre- vs. postprandial), drug condition (placebo vs. atropine), and trials (trial 1 vs. trial 2). Differences in compliance were determined by comparing the slopes for pre- and postprandial conditions (BMDP 1V) (3). Individual components of the compliance curves were further compared using repeated measures ANOVA. The index of distention-induced contractile activity was compared using a four-way ANOVA with repeated measures (BMDP 2V) (3); the factors were feeding condition (pre- vs. postprandial), drug condition (placebo vs. atropine), distention volume (baseline vs. predefecation), and experimental trials (trial 1 vs. trial 2). Significant interactions were followed by an evaluation of simple interaction effects as recommended by Winer (15). Descriptive statistics are presented as mean ± SEM. All comparisons were made at the 0.05 significance level.

RESULTS

As shown in Fig. 1, a significant drug × feeding interaction was found for distention volume, $F(1, 21) = 4.65$, $p < 0.05$. Following saline infusion, feeding significantly decreased postprandial defecation threshold. Atropine abolished the difference between pre- and postprandial defecation thresholds. A trend was seen for a reduction in the defecation threshold preprandially following atropine. This observation may suggest that atropine removes a tonic inhibition of the defecatory response. However, this effect failed to reach statistical significance, $F(1, 21) = 2.32$, $p < 0.05$. The consistency of these observations was supported by the lack of significant differences between the two independent trials, $F(1, 21) = 2.75$, $p = 0.11$.

Similar results were seen for pressure at defecation threshold. A significant drug × feeding interaction was found, $F(1, 21) = 6.40$, $p < 0.05$. Pressure was reduced postprandially following saline. Pre- and postprandial differences in defecation thresholds were abolished by atropine infusion (Fig. 2). There were no significant differences between the two trials, $F(1, 21) = 3.24$, $p = 0.09$.

Under placebo, compliance curves were similar in shape and in linear slope preprandially ($b = 0.15$) and postprandially ($b = 0.14$). Atropine had no significant effect on rectal compliance either preprandially ($b = 0.18$) or postprandially ($b = 0.16$). Analysis of variance revealed no significant differences between conditions for any distention volume.

The ANOVA for distention-induced contractile activity showed a significant two-way interaction, $F(1, 45) = 13.37$, $p < 0.05$, between drug conditions (atropine vs. placebo) and dis-

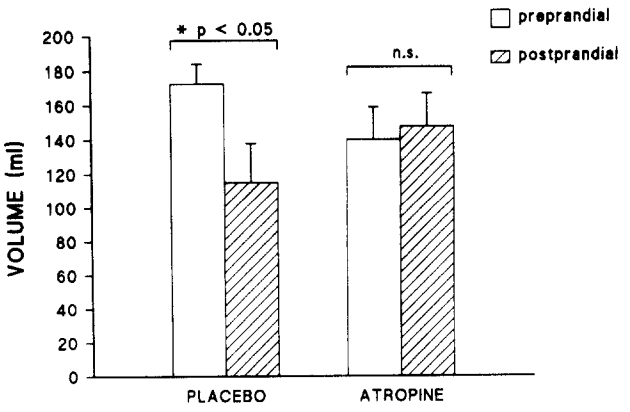

FIG. 1. Comparison between pre- and postprandial distention volume at defecation threshold for placebo and atropine (mean ± SEM).

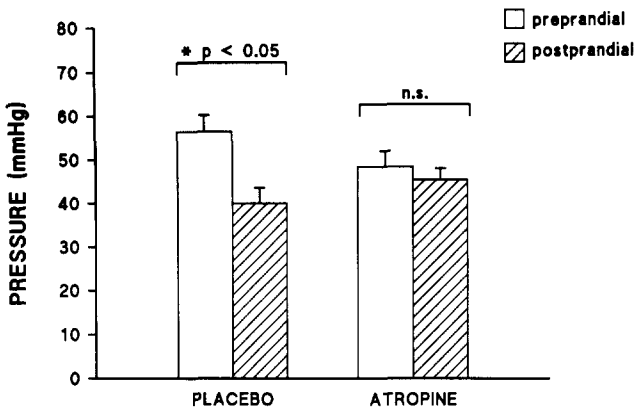

FIG. 2. Comparison between pre- and postprandial pressure at defecation threshold for atropine and placebo (mean ± SEM).

tention volumes (baseline vs. defecation threshold). Contractile activity increased with distention up to defecation threshold under both drug conditions. With saline infusion, the index of contractile activity increased from 1.29 ± 0.81 at baseline to 4.71 ± 1.71 at defecation threshold. Atropine did not affect the baseline index of contractility (1.64 ± 1.00), but significantly attenuated the motor response at defecation threshold (2.54 ± 1.74). There were no significant changes in the index of contractile activity as a function of feeding, $F(1, 45) = 2.04$, $p = 0.16$. The lack of a significant change in the index of contractile activity pre- and postprandially under placebo conditions suggests that the lowered postprandial defecation threshold was not a function of increased contractile activity.

DISCUSSION

Previous results showing a reduced defecation threshold in pigs were replicated (7). Under placebo conditions, the defecation threshold was reduced postprandially in terms of both distention volume and rectal pressure. Food intake had no significant influence on rectal compliance or distention-induced contractile activity. Changes in motor activity appeared to be a function of the distention volume (i.e., increasing with increasing volume). Atropine abolished the feeding-induced reduction in defecation threshold; pre- and postprandial conditions were not different. Atropine also attenuated the increase in distention-induced contractile activity seen under placebo conditions, but had no significant influence on rectal compliance.

Changes in distention-induced contractile activity were excluded as the mediator for the feeding-induced reduction in defecation threshold, since contractile activity under placebo conditions was not different postprandially compared to preprandially. Since this study only measured rectal motor activity under conditions of distention, no conclusions can be drawn concerning baseline changes in rectal motility associated with eating.

An alternative explanation for the lower postprandial defecation threshold under placebo conditions could be increased propagated contractions in higher parts of the colon that push stool forward into the rectum. In that case, postprandial defecation of the balloon should have been associated with the defecation of stool more often than under preprandial conditions. This hypothesis is unlikely, since defecation of stool with the balloon was equally distributed before and after feeding (16 vs. 20; $\chi^2 > 0.05$). Stool was consistently passed on the initial distention trials, which were not included in data analyses. This hypothesis cannot be excluded from these data. Further studies are necessary that measure contractile activity in the more proximal areas of the colon during rectal distention.

In humans, it has been shown that eating increases rectal tone (13) and that atropine counteracts this effect (2). We observed no difference in rectal compliance before or after the meal under either drug condition. These observations are not necessarily inconsistent, since they represent two distinct measures and there is no direct evidence that changes in resting tone affect compliance. Estimation of tone with a barostat (used in the human studies) requires only minimal distention of the gut wall, whereas estimation of compliance via balloon distention measures pressures following a provocative stimulus.

Our results are consistent with previous findings demonstrating that cholinergic pathways play an important role in mediating the early neural component of the gastrocolonic response. These results extend this observation to include a rectal response to eating, which includes the actual defecation response. Acetylcholine pathways appear to mediate both the colonic motor response to eating in humans (14) and the eating induced-defecation response in pigs.

The time course of the effect on defecation threshold under placebo conditions in our animals was similar to that reported by Erckenbrecht et al. (4) on the effect of eating on colonic perception in humans. They found that the volumes required to induce an urge to defecate were reduced during and immediately after eating. Since we have eliminated changes in distention-induced motor activity and compliance as likely explanations for the lower postprandial defecation threshold, our results could most parsimoniously be interpreted as a change in perception threshold that is part of a gastrorectal response resulting in volitional defecation and is mediated through cholinergic pathways.

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REFERENCES

1. Battle, W.; Cohen, S.; Snape, W. J. Inhibition of postprandial colonic motility after ingestion of an amino acid mixture. Dig. Dis. Sci. 25: 647–652; 1980.
2. Bell, A. M.; Pemberton, J. H.; Phillips, S. F.; Zinsmeister, A. F.; Hanson, R. B. Measurement of variations in human rectal tone. Gastroenterology 96:A38; 1989.
3. Dixon, W. J.; Brown, M. B.; Engelman, L.; Frane, J. W.; Hill, M. A.; Jennrich, R. I.; Toporek, J. D. BMDP statistical software. Berkeley, CA: University of California Press; 1983.
4. Erckenbrecht, J. F.; Lefhalm, C.; Wallstein, U.; Enck, P. The gastrocolonic response to eating is not only a motor but also a sensory event. Gastroenterology 96:A141; 1989.
5. Green, D. M.; Swets, J. Signal detection theory and psychophysics. New York: John Wiley & Sons, Inc.; 1966.

6. Levinson, S.; Bhasker, M.; Gibson, Th. R.; Morin, R.; Snape, W. J. Comparison of intraluminal and intravenous mediators of colonic response to eating. Dig. Dis. Sci. 30:33–39; 1985.
7. Musial, F.; Crowell, M. D.; French, A. W.; Whitehead, W. E. The effect of feeding on defecation behaviour in pigs. Physiol. Behav. 51:643–646; 1992.
8. Narducci, F.; Basotti, G.; Daniotti, S.; Del Soldato, P.; Pelli, M. A.; Morelli, A. Identification of muscarinic receptor subtype mediating colonic response to eating. Dig. Dis. Sci. 30:124–128; 1985.
9. Parker, R.; Whitehead, W. E.; Schuster, M. M. Pattern recognition program for analysis of colon myoelectric and pressure data. Dig. Dis. Sci. 32:953–961; 1987.
10. Renny, A.; Snape, W. J.; Sun, E. A.; London, R.; Cohen, S. Role of cholecystokinin in the gastrocolonic response to a fat meal. Gastroenterology 85:17–21; 1983.
11. Snape, W. J.; Wright, S. H.; Battle, W. M.; Cohen, S. The gastrocolonic response: Evidence for a neural mechanism. Gastroenterology 77:1235–1240; 1979.
12. Snape, W. J.; Matarazzo, S. A.; Cohen, S. Effect of eating and gastrointestinal hormones on human colonic myoelectrical and motor activity. Gastroenterology 75:373–378; 1978.
13. Steadman, C.; Phillips, S. F.; Camillieri, M.; Talley, N. J.; Haddad, A.; Hanson, R. Control of muscle tone in the human colon. Abstract FP1140. The World Congress of Gastroenterology, Sydney, Australia; 26–31 August 1990.
14. Sun, E. A.; Snape, W. J.; Cohen, S.; Renny, A. The role of opiate receptors and cholinergic neurons in the gastrocolonic response. Gastroenterology 82:689–693; 1982.
15. Winer, B. J. Statistical principles in experimental design, 2nd ed. New York: McGraw-Hill; 1962.