Rectal sensitivity assessed by a reflexologic technique: further evidence for two types of mechanoreceptors

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1Department of Gastroenterology, Institut National de la Santé et de la Recherche Médicale (INSERM) U-290, Saint-Louis and Saint-Lazare Hospitals, 75009 Paris; and 2INSERM U-161 and Pain Clinic, Ambroise Paré Hospital, 75014 Paris, France

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Sabate, Jean-Marc, Benoit Coffin, Raymond Jian, Daniel Le Bars, and Didier Bouhassira. Rectal sensitivity assessed by a reflexologic technique: further evidence for two types of mechanoreceptors. Am J Physiol Gastrointest Liver Physiol 279: G692–G699, 2000.—We previously showed that slow-ramp rectal distensions induce graded inhibitions of the somatic nociceptive RIII reflex recorded from the lower limb, which correlated with both distension volume and visceral sensation. In contrast, rapid phasic rectal distensions induced facilitatory or biphasic effects (i.e., facilitations followed by inhibitions) depending on the level of distension. To examine the role of mucosal and serosal rectal mechanoreceptors in these visceralosomatic interactions, we analyzed, in six healthy volunteers, the effects of both types of rectal distension on the RIII reflex after topical application of lidocaine or placebo administered in a double-blind and crossover fashion. Inhibitions of the RIII reflex induced by both slow-ramp and rapid distensions were strongly reduced after administration of lidocaine but not after placebo. In contrast, facilitations of the RIII reflex observed during the initial phase of rapid distensions were not modified after lidocaine or placebo applications. These results suggest that inhibitions, but not facilitations, of the nociceptive RIII reflex triggered by rectal distensions depend preferentially on the activation of superficial mucosal receptors. This reflexologic technique might thus represent an interesting tool for studying the role of the different rectal mechanoreceptors involved in visceral sensations.

pain; nociception; visceral perception; lidocaine

DIFERENT MECHANORECEPTORS of rectal and other visceral organs, involved in physiological or painful visceral sensations, seem to be preferentially activated by different patterns of inflation of hollow organs. It has been proposed that superficial mucosal and deeper musculoserosal mechanoreceptors are preferentially activated by slow-ramp and rapid phasic rectal distensions, respectively (17, 22). However, the respective contribution of these mechanoreceptors to rectal sensation remains difficult to assess in humans.

We developed a reflexologic technique based on the recording of a somatic nociceptive cutaneomuscular flexion reflex (i.e., RIII reflex) that might provide an interesting tool to assess somatovisceral interactions and visceral sensitivity more objectively in humans. This reflex is a polysynaptic reflex elicited by electrical stimulation of a cutaneous sensory nerve and recorded from a flexor muscle on the ipsilateral limb (23–25). The threshold and amplitude of this reflex response are closely related to those of concomitant painful cutaneous sensations evoked by electrical stimulation. We showed (3) in healthy volunteers that gastric distensions induced inhibitions of the reflex responses that closely correlated with both the volume of distension and the resulting visceral sensation. In a subsequent study (4), we observed that rectal distensions induced more complex effects depending on the site of recording of the reflex (i.e., upper or lower limb) and the mode of distension (i.e., rapid or slow ramp). Rapid rectal distensions facilitated the RIII reflex recorded from the lower limb, but at the highest distension level (i.e., 40 mmHg) facilitation was followed by inhibition. In contrast, slow-ramp distensions induced gradual inhibition of the RIII reflex that correlated with both the distension volume and the visceral sensation. We proposed that reflex inhibitions were probably related to the activation of spinal and/or supraspinal pain modulation systems. One plausible explanation for the facilitatory effects, which were not observed when the reflex was recorded at the upper limb, was that they were caused by the convergence of rectal and reflex afferents at the same levels of the spinal cord (4).

In any case, the differential effects of rapid and slow-ramp rectal distensions on the RIII reflex recorded from the lower limb suggested the activation of two functionally distinct populations of mechanoreceptors by these two modes of distension. The goal of the present study was to further characterize these phenomena and, in particular, to analyze the role of the different rectal mechanoreceptors. Using an experimental design similar to that in our previous study (4), we analyzed, in six healthy volunteers, the effects of slow-ramp and rapid phasic rectal distensions

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on the RIII reflex recorded from the lower limb after the topical application of the local anesthetic lidocaine or a placebo administered in a double-blind and crossover fashion.

**MATERIALS AND METHODS**

After approval by the local Ethics Committee, the experiments were performed on six healthy volunteers (4 men and 2 women, 27–40 yr old) with no evidence of chronic or acute illness or of gastrointestinal symptoms or altered bowel habits. Volunteers were carefully briefed about the experimental procedure and gave informed consent to participate.

**Nociceptive flexion reflex (RIII reflex).** The RIII reflex was elicited and recorded from the lower limb according to a previously described and validated technique (3, 4, 23–25). Briefly, the subjects were placed in a lateral decubitus position, and the RIII reflex was elicited and recorded by an entirely computerized system (Physio Labo System, Notocord, Igny, France). The sural nerve was electrically stimulated at a frequency of 0.17 Hz (10 stimulations/min) via a pair of surface electrodes placed 2 cm apart on the degreased skin overlying the nerve within its retromalleolar path. Each electrical stimulation consisted of a train of five constant-current pulses of 1-ms duration. Electromyographic responses were recorded from the ipsilateral biceps femoris via a pair of surface electrodes placed 2 cm apart on the degreased skin over the muscle. The RIII reflex response was identified as a multiphasic signal appearing between 90 and 180 ms after each stimulation. After amplification, each reflex response was digitized, full-wave rectified, and integrated. This integrated surface was used to quantify the RIII response. The RIII reflex threshold was defined as the average minimal current that elicited the reflex response. Before each experiment, this threshold was determined by four successive sequences of increasing and decreasing electrical stimuli. The intensity of electrical stimulation of the sural nerve was then adjusted to 20% above the threshold and kept constant during control, distension, and postdistension periods of each experimental sequence.

**Rectal distension.** An oversized spherical polyvinyl bag (10-cm maximal diameter, infinite compliance until maximal volume of 600 ml) was mounted on the tip of a double-lumen polyvinyl tube (12 Fr), folded tightly, lubricated, and inserted into the rectum. The distal attachment site was 4 cm from the anal verge. The tube was secured in its proper position with tape. The proximal opening of the tube was linked to an electronic barostat (INRA, Toulouse, France) that allowed controlled inflation and deflation of the balloon with air and continuous monitoring and recording of the volume and pressure inside the balloon. When in place, the balloon was unfolded by slowly injecting air under controlled pressure (<20 mmHg) and then completely deflated. After a 20-min period of rest, the barostat was used to inflate the balloon either rapidly (900 ml/min) to a constant pressure plateau (rapid phasic distension) or continuously at a constant volume rate of 40 ml/min (slow-ramp distension).

**Perception of rectal distensions.** Before the experiments, volunteers were informed of the visceral sensations they might experience. The sensation elicited by the rectal distension was graded from 0 to 6 using a verbal questionnaire: 0, no perception; 1, initial perception; 2, sensation of gas; 3, sensation of stool; 4, urge to defecate or onset of discomfort; 5, moderate pain; 6, intense or unbearable pain. In the case of rapid distension, subjects reported their sensations at the end of each distension period. In the case of slow-ramp distension, subjects reported their sensations at fixed intervals (every 50 ml of distension). Whenever intense or unbearable painful sensation (score 6) was experienced during any level of distension, the experiment was immediately suspended.

**Experimental design.** The six volunteers underwent experiments on four different days separated by an interval of 1 wk to test in each subject the effects of both rapid and slow-ramp distensions after the intrarectal application of lidocaine or placebo. The administration of lidocaine or placebo was performed according to a double-blind and crossover design, and the order of application of slow-ramp or rapid phasic distensions was randomized. All experiments were performed after a 12-h fast.

Each experimental day began with the determination of the RIII reflex threshold. Twenty milliliters of 2% viscous lidocaine (Astra Pharmaceuticals, Westborough, MA) or the same volume of placebo, a mixture of paraffin oil and saline, were then administered intrarectally, and the balloon was inserted. After a 20-min period of rest, a new determination of the RIII reflex threshold was performed and the rectal distensions were performed.

Rapid distensions were performed at four levels (10, 20, 30, and 40 mmHg) applied in a randomized order. Each distension was maintained for 3 min, and 10 min elapsed between the application of each level of distension to avoid sensitization phenomena. The RIII reflex responses were measured during the 3 min before distension (control period), during the 3-min distension period, and during the 3 min after distension (postdistension period).

Slow-ramp distensions were performed up to the pain threshold or the maximal volume of the balloon (600 ml). The RIII reflex responses were measured during the 3 min before distension (control period), during the continuous rectal distension period, and during a 3 min postdistension period. The RIII responses were averaged at 1-min intervals and expressed as a percentage of the mean value obtained during the control period. The sensations elicited by rectal distensions were scored as described in *Perception of rectal distensions*.

**Statistical analysis.** Results are expressed as means ± SE. The effects of the injection were analyzed using an ANOVA with the post hoc Newman-Keuls test, including classical effects for a crossover design: treatment, treatment order (placebo-lidocaine or lidocaine-placebo), and period (first or second stage). Relationships between two variables were tested by the Kendall rank correlation (τ). In all instances, *P* < 0.05 was considered significant.

**RESULTS**

**Effects of lidocaine on the RIII reflex.** The sural nerve stimulation at 1.2 times threshold elicited a fairly stable RIII response during the predistension period and evoked a moderate sensation of pain of the pinprick type, which was reported to originate from the level of the stimulating electrodes and to be projected up to the distal cutaneous receptive field of the sural nerve (external side of the foot). This sensation fluctuated minimally and was well tolerated throughout the experiments. The mean thresholds to evoke the RIII reflex were not significantly different before and after intrarectal application of saline (9 ± 1.5 vs. 9.3 ± 1.3 mA) or lidocaine (8.5 ± 2.6 vs. 8.2 ± 1.2 mA).

**Rapid distensions.** All volunteers completed the 10-, 20-, and 30-mmHg levels of distension with lidocaine and saline. However, only three volunteers could tol-
erate the 40-mmHg level of distension, one with both saline and lidocaine, two only with lidocaine. This level of distension was not considered in further analysis of the results. An example of the effects of rapid distensions on the RIII reflex after topical application of placebo (A–C) or lidocaine (D–F). Each bar represents a single reflex response, expressed as % of the mean value for the 3-min predistension control period. Arrows delimit the 3-min period of distension.

Fig. 1. Individual example showing the effects of rapid rectal distensions from 10 to 30 mmHg on RIII reflex recorded from the lower limb after the intrarectal application of placebo (A–C) or lidocaine (D–F). Each bar represents a single reflex response, expressed as % of the mean value for the 3-min predistension control period. Arrows delimit the 3-min period of distension.

The cumulative data observed in the six volunteers are shown in Fig. 2. The RIII reflex was not significantly modified during the 10-mmHg distension performed after both lidocaine and placebo. The effects observed during the first minute of the 20- and 30-mmHg distensions for the six volunteers were not different after placebo (116 ± 9% and 109 ± 16% of control values, respectively) and lidocaine (116 ± 12% and 117 ± 11% of control values, respectively). Clear facilitations of the RIII reflex, up to 156% of control values, were observed during the first minute of distension in four of six subjects and were not significantly different after the administration of placebo (128 ± 6.2% and 125 ± 5.1% of control values for 20- and 30-mmHg distensions, respectively) or lidocaine (133 ± 7.2% and 129 ± 4.3% of control values for 20- and 30-mmHg distensions, respectively). Inhibi-
tions of the RIII reflex were observed during the second and third minutes of the 20- and 30-mmHg distensions after placebo (66.7 ± 10.6% and 54.9 ± 15.5% of control values, respectively). These inhibitions were significantly reduced after lidocaine (113.1 ± 12.7% and 87.3 ± 12.5% of control values, respectively; P < 0.05 for the comparison between placebo and lidocaine).

**Slow-ramp distension.** All volunteers completed this series after both placebo and lidocaine administration. Examples of the effects of slow-ramp rectal distensions on the RIII reflex in the presence of placebo or lidocaine are shown in Fig. 3, A and B, and the cumulative data are shown in Fig. 3C. The mean duration of slow-ramp distension was 12.3 ± 0.6 min after placebo and 14.3 ± 1.4 min after lidocaine administration. Slow-ramp distension performed after placebo induced a graded inhibition of the RIII response that became significant at a volume of 120 ml and was correlated with the volume of distension (Kendall τ = 0.53; P < 0.001). Such inhibitions were strongly reduced after lidocaine administration. The mean RIII response at the maximal volume of distension was significantly different between slow-ramp distensions performed after placebo and lidocaine administration. As shown in Fig. 4, the inhibition of the RIII reflex was correlated with rectal sensation after placebo (Kendall τ = 0.49, P < 0.001) but not after lidocaine administration.

**Effects of lidocaine on visceral sensation and rectal compliance.** The mean sensation scores elicited during the 10-, 20-, and 30-mmHg rapid distensions were correlated with the distension level and were not significantly different after placebo (1.5 ± 0.3, 3.6 ± 0.4, 4.3 ± 0.1, respectively) and lidocaine (1.7 ± 0.2, 3.0 ± 0.4, 4.1 ± 0.3, respectively) administration (Fig. 5B).

During slow-ramp distension, a significant correlation was evidenced between the level of distension and sensation scores after both placebo and lidocaine. However, rectal sensations were significantly decreased after lidocaine (P < 0.02; Fig. 5D).

Compared with placebo, lidocaine did not modify rectal compliance either during rapid phasic distensions (Fig. 5A) or during slow-ramp distensions (Fig. 5C).

**DISCUSSION**

The present results show that inhibitions of the nociceptive flexion (RIII) reflex and the visceral sensations elicited by slow-ramp rectal distensions were strongly reduced after intrarectal application of lidocaine. In contrast, facilitations of the RIII reflex were observed at higher volumes of slow-ramp distensions performed after lidocaine administration. These data thus seem to confirm that two functionally distinct types of rectal mechanoreceptors are activated by these different modes of distension.

Several lines of evidence suggest that rapid phasic and slow-ramp rectal distensions preferentially activate distinct sets of receptors and afferent pathways. In normal subjects, discomfort thresholds are higher during phasic distension than during slow-ramp distension (17, 22). Abnormal sensory responses were reported in patients with irritable bowel syndrome (IBS) during rapid phasic distension but not during slow-ramp distension (17, 19, 20). Topical application of lidocaine decreases the sensation elicited by slow-
ramp distension in healthy subjects and in some patients with IBS but has no effect on sensation elicited by phasic rapid distension in either group (16). Octreotide increases rectal perception thresholds during slow-ramp but not phasic distension (19). On the basis of these results and those of anatomic and electrophysiological studies in animals (6, 7, 11–13, 21), it has been hypothesized that sacral afferents connected with mucosal mechanoreceptors are preferentially stimulated during slow rectal distensions, whereas splanchnic afferents, whose receptive fields are in the serosa and mesentery and project to the lumbar spinal cord, are preferentially activated during rapid distensions (16, 17). The fact that patients with complete lesions of the lower spinal cord do not perceive slow-ramp rectal distension, although they still perceive phasic stimuli (16), is in accordance with such a hypothesis. It should be emphasized, however, that the specific effects of these two kinds of distension still remain controversial. Animal experimental data indicate that phasic distensions of the hindgut can stimulate both parasympathetic and splanchnic afferents (11). Studies performed in humans are also conflicting. Plourde et al. (19)
concluded that the friction of the balloon during slow-ramp distension preferentially stimulates rapidly adapting mucosal receptors, whereas the activation of the muscular mechanoreceptors is limited by reflex relaxation. In contrast, Sun et al. (22) concluded that this mode of distension preferentially activates slowly adapting mechanoreceptors. These discrepancies could have been caused by the fact that most of the studies on this topic were based on the evaluation of subjective sensory thresholds. The present data based on a reflexologic technique might provide a more objective way of confirming the functional duality of rectal mechanoreceptors.

Our main finding was that lidocaine strongly reduced inhibitions of the RIII reflex induced by both slow-ramp and rapid phasic rectal distensions. Such viscerosomatic inhibitory interactions have been described in animals (5, 18). They probably involve supraspinal and/or segmental systems that modulate the spinal transmission of nociceptive signals. There is little information concerning these modulatory systems in humans. However, one of these systems, diffuse noxious inhibitory controls, which was initially described in the rat (14, 15), has also been demonstrated in humans (10, 24, 25). On the basis of the present results it can be proposed that these inhibitory phenomena mainly depend on the activation of mucosal mechanoreceptors, which is obviously attenuated by the application of local anesthetics (2, 8). It is not known, however, how deeply the anesthetic penetrates the rectal wall and how much of the administered dose is absorbed (9). In a study performed under conditions similar to those of the present study (16), motor reflex responses that do not involve mucosal tension receptors (i.e., anorectal inhibitory reflex and receptive relaxation) were not affected by lidocaine, suggesting that its action was limited to the superficial mucosa. Accordingly, the lack of effects of lidocaine on the pressure-volume relationship observed in the present study suggests that muscular and serosal receptors were probably not affected by lidocaine. In addition, the lack of changes of the RIII reflex threshold after lidocaine argues against a systemic diffusion of the drug.

Similar to the findings of our previous study (4), a strong correlation was evidenced between the inhibition of the RIII reflex responses and the visceral sensations induced by slow-ramp distensions performed after administration of the placebo. Such a correlation was not observed after administration of lidocaine. The inhibitory effects on the RIII reflex were blocked, but, interestingly, the sensations during slow-ramp distensions were reduced but not completely abolished after lidocaine. This residual sensation might have been encoded by muscular or serosal mechanoreceptors whose function was not altered by lidocaine. It is thus
possible that not only the mode of stimulation but also the intensity of the stimulus should be taken into account, because deeper receptors with receptive fields in the serosa could also be activated when slow-ramp distensions reach high volumes. This might explain why in some volunteers inhibitions of the RIII reflex induced by slow-ramp distensions were replaced by facilitations at higher volumes of distensions after lidocaine.

Inhibitions of the RIII reflex were also observed during the plateau phase of the rapid distensions performed after placebo administration. These inhibitory effects were more pronounced than those we previously observed (4) under similar experimental conditions. They were observed during the 20- and 30-mmHg distensions, whereas in our previous study they were observed only during the 40-mmHg distension. We do not have a satisfactory explanation for these discrepancies. The shearing forces applied by the balloon on the rectal wall could have been modified by the intrarectal administration of the placebo or lidocaine. Alternatively, the residual volume of the injections within the rectum could have decreased distensibility. Such a volume effect might explain why, in the present study, a majority of the volunteers were not able to tolerate the 40-mmHg distension after both placebo and lidocaine. In any case, the inhibitions observed during phasic distensions were also probably dependent on the activation of superficial receptors, because they were reduced after lidocaine administration. In fact, one can speculate that the rapid rise of muscle tension preferentially activates splanchnic afferents with receptive fields located in the muscle and the serosa but that mucosal afferents can also be activated by the shearing effects of the balloon during the plateau phase of the distension (1).

The RIII reflex was facilitated during the initial phase of the 20- and 30-mmHg rapid distensions, and these facilitations were not different after administration of the placebo or lidocaine. On the basis of our previous study showing that such facilitatory effects were not observed during the recording of the RIII reflex from the upper limb, we proposed that they could be explained by the convergence onto the same spinal segments of the rectal afferents and those of the RIII reflex, which is integrated in the lumbar and sacral levels of the spinal cord (4). The fact that the facilitations of the RIII reflex were not affected by lidocaine is in accordance with such a hypothesis. It is suggested that these facilitatory phenomena were not mediated by the stimulation of superficial receptors but rather by splanchnic afferents projecting within the lumbar spinal cord. It is likely, however, that the inflation pattern that we used during rapid phasic distensions preferentially activated muscular or serosal mechano-receptors only during the initial phase of the distension. Indeed, facilitations of the RIII reflex were mainly observed during the first minute of the distension, whereas inhibitory effects were observed during its plateau phase. Alternatively, we cannot exclude that reflex relaxation and muscle accommodation were triggered during the plateau phase of the distension, explaining, at least in part, why the facilitatory effects were observed only during the initial phase of the distension. Thus a limitation of our experimental paradigm for the comparison of the effects of slow-ramp and rapid distensions could have been the relatively long duration of the plateau of the rapid distensions, which in fact were rather “phasicotonic.” In future studies using this methodology to compare the effects of the two modes of distension, it would probably be more appropriate to perform rapid distensions over only 1 min.

In conclusion, the present results strongly suggest that the differential effects of rectal distensions on the nociceptive flexion RIII reflex are caused by the activation of distinct sets of rectal mechanoreceptors by different inflation patterns. This reflexologic technique might thus provide an interesting tool for evaluating more objectively the respective contribution of superficial and deeper receptors in visceral sensory disorders as well as in pharmacological studies.

REFERENCES


