Objective: Abdominal surgery invariably causes a temporary reduction of normal intestinal motility, called postoperative ileus. Postoperative ileus extends hospital stays, increases the costs of hospitalization, and may contribute to the formation of postoperative adhesions. We designed experiments to determine if visceral massage affects postoperative ileus in a rat model.

Material and methods: Forty female Long Evans rats were assigned to 4 groups in a 2 (surgery) × 2 (treatment) factorial design. Twenty rats were subjected to a small intestinal manipulation designed to emulate “running of the bowel.” Transabdominal massage was performed upon 10 operated and 10 control rats in the first 12 h following surgery. Ileus was assayed after 24 h using fecal pellet discharge and gastrointestinal transit. Intraperitoneal inflammation was assayed using total intraperitoneal protein and inflammatory cell concentrations.

Results: The surgery consistently caused ileus. Compared to the operated group with no treatment, the operated with treatment group showed increased gastrointestinal transit and reduced time to first fecal pellet discharge. Similar group comparisons revealed that the treatment decreased total intraperitoneal protein and numbers of intraperitoneal inflammatory cells.

Conclusions: In this rat model, visceral massage reduced experimental postoperative ileus. The data suggest that the effect was through the attenuation of inflammation. A similar study could be designed and performed in a hospital setting to assess the potential role of visceral massage as part of the integrated care for postoperative ileus.

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Introduction

Abdominal surgery invariably causes a temporary reduction of intestinal motility, called ileus. Ileus is characterized by a lack of coordinated intestinal activity and a substantial overall reduction in peristalsis, and is an important cause of postoperative discomfort and prolonged hospital stays (Bauer, 2010; Mattei and Rombeau, 2006; Person and Wexner, 2006). The increased number of days spent in the hospital places a huge financial burden on health care delivery systems (estimated to be $0.75 billion per year in the United States for colectomies alone) (Doory and Senagore, 2012; Iyer et al., 2009; Johnson and Walsh, 2009; Senagore, 2010). There remains no fully effective treatment for ileus (Bauer, 2010; Engel et al., 2010; Mattei and Rombeau, 2006; Zeinali et al., 2009), although recent advances have been made by combining ileus-limiting approaches such as laparoscopic surgery, epidural anesthesia, pain management, and new drugs (Johnson and Walsh, 2009; Kraft, 2009; Person and Wexner, 2006). The concept that visceral or abdominal massage could attenuate ileus was first published more than a century ago (Coe, 1899; Haberlin, 1899), but the topic received little further consideration. More recently, abdominal massage using a mechanical device was shown to reduce ileus (Le Blanc-Louvy et al., 2002). A systematic review supported that osteopathic manipulative treatment reduced ileus (Crow and Gorodinsky, 2009), however, there were few details related to the treatment methods, and it cannot be gleaned whether the abdomen was directly treated. Other supportive data include that visceral massage is effective for constipation (Ernst, 1999; Klauser et al., 1992; Lamas et al., 2009), and that it increases bowel function in spinal cord injured patients (Ayas et al., 2006; Liu et al., 2005).

We recently described the effects of visceral massage on postoperative adhesions in a rat model (Bove and Chapelle, 2012). During these experiments, we observed that the rats, who were fully accommodated to handling, consistently defecated during or soon after visceral massage, suggesting a prokinetic effect on the intestines. We designed the current study to determine if visceral massage would decrease ileus in a rodent model of postoperative ileus. Because inflammation has been shown to be the key to postoperative ileus (Bauer, 2010; Mattei and Rombeau, 2006; Tracey, 2002; Wehner et al., 2007), we also performed assays of intraabdominal inflammation to determine possible associations with visceral massage.

Materials and methods

Animals and surgery

All procedures were consistent with the Guide for the Care and Use of Laboratory Animals (National Research Council, USA), and were approved by the University of New England Institutional Animal Care and Use Committee. Forty adult, female Long Evans rats were obtained from Charles River Laboratories (USA), and weighed 225 g when used. Rats in the surgery group were anesthetized with isoflurane in pure oxygen (4% for induction, 2% for maintenance), and their abdominal walls were shaved and scrubbed with betadine and 70% isopropanol. The surgical field was draped and surrounded with sterile saline-soaked gauze. A 3 cm vertical incision was made just lateral to the linea alba. The small intestine from the distal duodenum to the distal ileum was gently exteriorized using gloved fingers. Starting with the distal duodenum and moving distally, the entire small intestine was gently rolled between the thumbs and forefingers, enough to compress and move the luminal contents, but not enough to fully occlude the lumen or cause bleeding. This process took 5 min. The small intestine was then covered with saline-soaked gauze, left for 10 min, and then returned to the abdominal cavity. The incision was sutured in layers (4-0 Monoweb; Webster Veterinary, USA). The rats were injected subcutaneously with morphine sulphate (0.3 mg/kg s.c.), and wrapped in a soft pad for recovery. To control for the effects of the morphine, all rats not subjected to surgery were also injected with morphine sulphate (0.3 mg/kg s.c.) at the onset of the experiment. The rats not subjected to the surgery were not anesthetized, because inhaled anesthetic agents do not interfere with gastrointestinal function after their cessation (Condon et al., 1987).

Experimental design

Ten rats were randomly assigned to each of 4 experimental groups in a 2 × 2 design: Surgery/Treatment (ST), Surgery/No Treatment (SNT), No Surgery/Treatment (NST), and No Surgery/No Treatment (NSNT). The start of the experiment was defined as the time when the rats were injected with morphine. Rats were placed in separate enclosures for the duration of the experiment to facilitate fecal pellet counts, with free access to food and water. The endpoint for all rats was 24 h after the start of the experiment.

Treatment

Rats in the treated groups (ST and NST) were removed from the cage and turned supine. One massage therapist (SLC) performed all the treatments, which standardized the procedures. SLC is a Registered Massage Therapist trained in Canada, with 18 years experience, who has focused much of her practice on postoperative care. The massage treatments consisted of gentle mobilization for 1 min. Treatments started with a side to side motion using the index finger and thumb placed lateral to the descending and ascending colon, respectively, for approximately 15 s. After mobilization, treatment continued by massaging in small circles with the index finger over the ascending, transverse, and descending colon in a clockwise pattern, starting from the bottom right abdominal quadrant to the bottom left abdominal quadrant, for approximately 45 s. These maneuvers were intended to mobilize the small and large intestines and encourage metabolite exchange within the intraperitoneal fluid. Treatments were performed at 15-min intervals for the first hour (4 treatments), at 30-min intervals for the next 2 h (4 treatments) and every 2 h thereafter until 12 h postoperatively (4 treatments). Rats in the non-treated groups (SNT and NSNT) were picked up and handled for approximately 1 min to...
control for possible non-specific effects of the treatment, on the same schedule that the rats in the other groups were treated.

**Outcome measurements**

Outcome measurements included time to first fecal pellet discharge; fecal pellet counts at 6, 12, and 24 h; gastrointestinal transit time; intraperitoneal fluid total protein concentration; and numbers of intraperitoneal inflammatory cells. After counting fecal pellets at 24 h, rats were lightly anesthetized and gavaged with ~1 ml of a slurry of 10% charcoal and 1% arabic acid in water, to measure gastrointestinal transit time. After 30 min, rats were anesthetized with isoflurane, followed by replacement of the gases with pure CO₂ to cause death. A small incision was made in the proximal abdominal wall, and 2 ml sterile phosphate buffered saline was injected into the peritoneal cavity. The abdominal contents were gently mobilized for 10 s, and the incision widened. Lavage fluid was collected with a gavage needle, and placed in vacutainers coated with EDTA. The small intestine was removed en bloc from the pylorus to the ileocecal valve, and carefully placed along a tape measure. The length from the pylorus to the ileocecal valve was measured and recorded. The distance from pylorus to the most distal visible charcoal was also measured, and used to calculate the gastrointestinal transit over 30 min (expressed as percentage of total small intestine length). The collected lavage fluid was then centrifuged, and the supernatant aspirated and used to assay total protein using a BCA protein assay (Pierce-Thermo Scientific, USA). The pellet containing cells was washed and suspended in phosphate buffered saline, and the numbers of cells were quantified using a standard hemocytometer. Trypan blue was added to differentiate live from dead cells.

**Data analysis**

All data other than cumulative fecal pellet discharge were analyzed using 2 (surgery) × 2 (visceral massage) ANOVAs (JMP 8.0 for Macintosh; USA). Cumulative fecal pellet discharge data were analyzed using a multivariate ANOVA (surgery, visceral massage, time). Analyses were followed by Tukey’s HSD post-hoc tests when appropriate. Time to first fecal pellet discharge was measured in minutes and reported in hours. Fecal pellet discharge during the first 15 min following anesthesia removal, or induced by the morphine injection procedure, was disregarded. If there was no discharge after 12 h, it was recorded as 12 h (n = 5). Alpha levels were set to 0.05.

**Results**

Although all rats in the treatment and non-treatment groups were initially given a low dose of morphine to simulate postoperative ileus scenarios, no further drug or restraint was necessary. None of the rats struggled, vocalized, or bit during any treatment, consistent with our previous experiences (Bove and Chapelle, 2012). The therapist reported that the abdomens of the rats that had undergone surgery had a deeper resistance to movement than the unoperated rats.

**Ileus model**

Surgery significantly reduced gastrointestinal transit [main effect of surgery; F(1, 33) = 12.31, p < 0.001; Figure 1A], and reduced fecal pellet discharge [main effect of surgery; F(1, 34) = 5.36; p < 0.05; Figure 1B]. There was no effect of surgery on the time to first fecal pellet discharge [F(1, 33) = 0.11; p > 0.10]. These data support that the surgical procedure consistently induced ileus. To determine if ileus remained after 24 h, the fecal pellet discharge of another group of 10 normal rats was observed (these data were not included in the statistical analysis). The comparison supported the presence of residual ileus after 24 h in all 4 experimental groups (Figure 1B). This was likely to have been caused by the morphine.

**Effect of treatment on gastrointestinal function**

There was a main effect of visceral massage on gastrointestinal transit [F(1, 33) = 12.56, p < 0.001, Figure 1A]. Post-hoc tests supported that visceral massage led to significant increases in small intestine transit in the surgery and treatment (ST) group compared to the surgery group of 10 normal rats (NORM), is depicted to demonstrate the probable contribution of morphine to ileus in all experimental groups. C. Visceral massage significantly reduced the time to first fecal pellet discharge. All noted differences were statistically significant by ANOVA (see text for details). Data are presented as means ± SEM.

![Figure 1](image-url)
with no treatment (SNT) group (Tukey’s HSD, $p < 0.05$, Figure 1A). Although there was no main effect of treatment on cumulative fecal pellet discharge, there were significant interactions between time and surgery (MANOVA, $p < 0.005$, Figure 1B), time and treatment ($p < 0.01$), and time, surgery, and treatment ($p < 0.05$), indicating that over time there was increased discharge due to the treatment. Treatment reduced time to first fecal pellet discharge [main effect; $F (1, 33) = 11.36; p < 0.01$; Figure 1C], which was also independent of whether surgery had been performed (there was no interaction between treatment and surgery; $F (1, 33) = 1.24; p > 0.10$). These data support that visceral massage significantly increased gastrointestinal function, and reduced postoperative ileus.

### Effect of treatment on total intraperitoneal protein and leukocyte concentrations

To test the possibility that visceral massage may reduce ileus through a suppressing effect on inflammation, we performed peritoneal lavage on all rats just following death, and assayed the concentrations of total protein and numbers of inflammatory cells (leukocytes). There was a main effect of surgery on total intraperitoneal protein [$F (1, 36) = 49.08; p < 0.001$; Table 1 and Figure 2A]. There was no main effect of treatment [$F (1, 36) = 0.01, p > 0.10$] but there was a significant interaction between the surgery and treatment [$F (1, 36) = 7.19; p < 0.01$]. This highlighted that the effect of the treatment differed depending on whether surgery had been performed or not performed. Post-hoc tests were not significant. The surgical procedure caused a large increase in the number of inflammatory cells compared to normal animals [main effect; $F (1, 36) = 5.40; p < 0.05$; Table 1 and Figure 2B]. Although there was no main effect of the treatment [$F (1, 36) = 0.87; p > 0.10$], there was an interaction between the surgery and treatment [$F (1, 36) = 10.93; p < 0.005$], supporting that the effect of the treatment differed in the surgical versus nonsurgical groups. Post-hoc tests supported that visceral massage led to a significant reduction in the number of intraperitoneal cells in the ST group compared to the SNT group (Tukey’s HSD, $p < 0.05$).

### Discussion

Our results indicated that visceral massage attenuated postoperative ileus in this rat model. Massage significantly increased gastrointestinal transit, augmented cumulative fecal pellet discharge, and shortened the time to first fecal pellet discharge. The comparison to a normal group of rats suggested that ileus was maintained for 24 h. Because of the chosen endpoint, it is not known whether the treatment affected the time to complete ileus resolution; this could be addressed in a future study.

We considered that the effects of massage on postoperative ileus could be simply mechanical; in other words, did the treatment simply push the intestinal contents along? This is very unlikely: directional propulsion of the intestinal contents requires peristaltic waves, which are highly coordinated. Mechanical effects of massage would not likely be unidirectional, especially in the small intestine, where the contents are more liquid than solid and where we measured effects. Furthermore, the improvement 12 h past the time of treatment cessation indicated a lasting stimulatory effect of massage on postoperative ileus, arguing against simple mechanical effects. However, the possibility that the massage triggered effective peristaltic activity of the large intestine is supported by a case report of a patient with spastic paralysis of the bowel, where self-administered abdominal massage evoked transient rectal peristaltic waves (Liu et al., 2005).

Intraperitoneal inflammation is currently held to be key to prolonged postoperative ileus (Bauer, 2010; Mattei and Rombeau, 2006; Wehner et al., 2007). Increased parasympathetic activity decreases intraperitoneal inflammation by inhibitory actions that have been collectively called the “inflammatory reflex” (for reviews, see Tracey, 2002, 2007, and Van Der Zanden et al., 2009), and has been shown to ameliorate postoperative ileus (de Jonge et al., 2005; The et al., 2007). We show that intraperitoneal protein concentration and inflammatory cell numbers were reduced by visceral massage, indicating a dilution of the inflammatory milieu. Although the mechanisms of visceral massage’s effects on intraperitoneal inflammation are unknown, it is proposed that the reduction we observed was reflex-mediated, through the vagus nerve. Inflammation sensitizes sensory receptors and axons to mechanical stimuli (Beyak and Vanner, 2005; Boye et al., 2003; Habler et al., 1988; Koda and Mizumura, 2002), but ileus reduces mechanical stimuli to the gut sensory system. It is likely that the mechanical stimuli of the massage increased afferent input in this sensitized system. Reflexively, increased afferent drive in this pathway will result in increased parasympathetic activity to the affected area (reviewed by Tracey, 2002). Interestingly, both total protein and leukocyte numbers increased in rats not subjected to surgery, suggesting that under normal conditions, the treatment is somewhat proinflammatory. This is consistent with the fact that in the absence of pathology, intraperitoneal receptors are relatively insensitive, and thus would not be expected to initiate a substantial reflexive response from the parasympathetic system. A future study could be designed to investigate the role of vagal reflexes in the effects of massage on ileus.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Protein (mg/ml)</th>
<th>Cells/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSNT</td>
<td>3.55 (0.63)</td>
<td>917 (249)</td>
</tr>
<tr>
<td>NST</td>
<td>5.78 (0.47)</td>
<td>5673 (2293)</td>
</tr>
<tr>
<td>SNT</td>
<td>11.82 (1.13)</td>
<td>12,192 (3190)</td>
</tr>
<tr>
<td>ST</td>
<td>9.47 (1.01)</td>
<td>3708 (736)</td>
</tr>
</tbody>
</table>

All data are presented as mean (±SEM). NSNT = No Surgery, No Treatment; NST = No Surgery, Treatment; SNT = Surgery, No Treatment; ST = Surgery, Treatment. Protein concentration and cells/ml data are graphically depicted in Figure 2. See text for details on Statistical analysis.
It has also been proposed that postoperative adhesions, a side effect of most abdominal surgery (Parker et al., 2007; Stanciu and Menzies, 2007), are fostered by ileus (Fu et al., 2005; Springall and Spitz, 1989). We have previously shown in a rat model that a visceral massage immediately following surgery interfered with the formation of postoperative adhesions (Bove and Chapelle, 2012). It follows that a reduction in postoperative ileus may limit adhesion formation by promoting normal peristaltic movements, although these beneficial effects could also be due to passive motion of the intestines while normal peristaltic motions recover.

Assumptions could be made that in humans, postoperative abdominal pain and sensitivity will preclude such treatment; this assumption was also made regarding treating the rats prior to performing these experiments. Our therapist's experience with humans, and now with rats, support that visceral massage is welcomed. It has also been suggested that such mechanical stimulation could disrupt intestinal surgical repairs. This notion has no experimental support, but our preliminary observations with an experimental end–end colonic anastomosis in rat support that vigorous visceral massage does not disrupt even very delicate sutures. This should be addressed in a future study. With appropriate precautions, including clear communication with the physician regarding the procedures performed, care to prevent infections, and maintaining constant feedback from the conscious patient, gentle mobilization of the abdominal cavity immediately postoperatively should be safe.

The methods used in this study were scaled—down versions of methods currently in routine use with humans, based on our therapist's best estimation and broad experience. Visceral massage, for constipation (Ernst, 1999; Lamas et al., 2010) and other complaints, is a standard part of massage therapy education in North America (Kellogg, 1895; Salvo, 2009), and massage therapy is part of massage therapy education in North America (Lamas et al., 2010) and other countries, is a standard practice. It will catalyze such a study, which has the potential to reduce hospital stays, improve overall outcomes for abdominal and pelvic surgical patients, and reduce hospitalization costs.

Acknowledgments

Disclosures: Financial assistance for this project was provided in part through a seed grant from the Massage Therapy Association of British Columbia to GMB and SLC. The authors acknowledge the generous assistance of Dr. Michael Burman, Dr. Ling Cao, and Ms. Jennifer Malon.

References


