Long-Term Effects of Jejunoileal Autotransplantation on Myoelectrical Activity in Canine Small Intestine

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We studied the longitudinal effects of autotransplantation on the motor function of the jejunoileum. By performing the autotransplantation procedure in a manner similar to that employed for allotransplantation, we sought to examine the long-term effects of both extrinsic denervation and the operative procedure itself on small intestinal motor function. Although initially disrupted, interdigestive myoelectrical activity demonstrated progressive organization: 88% of migrating myoelectrical complexes in animals studied between 12 and 20 months following autotransplantation demonstrated each phase of the complex in normal sequence. Longitudinal studies of several parameters of myoelectrical activity provided further evidence of progressive organization and entrainment of motor functions within the denervated intestine. Several abnormal myoelectrical patterns were observed within the autotransplanted segment, however, and coordination of either slow wave or phase III activity with the proximal innervated intestine did not recover with time. The major component of the myoelectrical response to feeding was permanently impaired with a delayed onset and shortened duration of the fed response. We conclude that the extrinsically denervated intestine recovers the ability to generate and organize all phases of the MMC but demonstrates permanent impairment of the major motor response to food. However, anoxic and cooling damage to enteric nerves and muscle, incurred during the autotransplantation procedure, may explain the persistence of abnormal motor patterns and impaired myoelectrical conduction and could play an important role, additional to that of extrinsic denervation, in the long-term motor function of the allotransplanted intestine.

KEY WORDS: intestinal motility; intestinal myoelectrical activity; autonomic nerves; neural control; gut function; small intestinal transplantation; migrating myoelectrical complex; intestinal ischemia.
matic autonomic neuropathy (4). Long-term persistence of such motor disruption could adversely affect intestinal absorptive function and thereby jeopardize the prospects for independent survival of the transplanted patient.

Given that it involves complete transection of all sympathetic and parasympathetic fibers to the autotransplanted gut, this model also provides insights into the role of the extrinsic nervous system in the control of intestinal function and contributes to our understanding of the pathophysiology of autonomic neuropathies. Studies to date suggest that, while the autotransplanted bowel can generate migrating motor complexes, other aspects of interdigestive motility are abnormal, and the motor response to feeding is impaired (3, 5–9). Uncertainty exists, however, as to the permanence of these abnormalities and to the potential of the autotransplanted intestine to develop, with time, coordinated motor responses in the absence of extrinsic innervation.

Our aim, therefore, was to study the long-term effects of autotransplantation on canine jejunoileal myoelectrical activity. Performance of allotransplantation also necessitates temporary isolation of the donor intestine from vascular perfusion and its placement in cold preservation solution pending implantation in the recipient; circumstances that could lead to either anoxic or cold injury to enteric nerves or gut muscle. In this study we sought, therefore, to reproduce, as closely as possible, the circumstances of allotransplantation.

MATERIALS AND METHODS

Preparation of Animals and Postoperative Care

All studies were performed on adult female mixed-breed dogs weighing between 15 and 20 kg. For all surgical procedures, animals were premedicated with intravenous acepromazine (Promace, Aveco Co., Inc., Fort Dodge, Iowa) in a dose of 20 mg. Anesthesia was achieved with intravenous pentobarbital (Nembutal, Abbott Labs, North Chicago, Illinois) in a dose of 30 mg/kg, and animals were maintained on a room air ventilator during the surgical procedure.

Autotransplantation. In animals selected to undergo autotransplantation of the jejun ileum (N = 14), the small intestine from the ligament of Treitz to within 5 cm of the ileocecal valve was isolated on a vascular pedicle comprising the superior mesenteric artery and vein; care was taken to preserve the arterial and venous supply to the pancreas and duodenum. At the proximal and distal ends of the segment, the intestine was transected with a surgical stapler and the mesentery to the segment freed. The superior mesenteric artery then was divided and the entire segment removed and placed in a bath of saline maintained at 4°C for a period of 30–45 min. The external iliac artery and vein was isolated and the jejun ileum reimplanted. To facilitate the reanastomosis, the proximal 5 cm of both the superior mesenteric artery and vein supplying the jejun ileum were skeletonized; all adherent tissues (including nerves and lymphatics) were cleared from both vessels down to the level of the adventitia. The superior mesenteric artery was anastomosed to the aorta and the superior mesenteric vein to the vena cava. Intestinal continuity was restored by end-to-end anastomosis.

Control. In a separate group of five animals (control, C), intestinal continuity and innervation remained undisturbed. Electrodes were placed, at laparotomy, at sites similar to those of the animals with autotransplanted jejun ileum (see Electrode Placement, below).

For 48 hr postoperatively each AT animal received 1 liter of 5% dextrose in 0.5 N NaCl every 24 hr. Oral 3 oral feedings were commenced with 473 ml (16 fl oz)/day of a complete liquid nutrition formulation, which provided a total of 2 kJ (480 calories) daily (Isocal, Mead Johnson Nutritional, Evansville, Indiana, osmolality 300 mosm/liter; 13% of calories as protein, 37% as fat, and 50% as carbohydrate). On the sixth day regular kennel chow was offered and increased as tolerated. Supplemental liquid nutrition formula was continued until the animal could be maintained on regular kennel chow alone.

Electrode Placement

Subserosal electrodes were placed at a second laparotomy performed at a variable interval following autotransplantation. To provide a longitudinal profile of the myoelectrical patterns over a time period ranging from one to 20 months from autotransplantation, electrode placement was performed in three groups. In the first group, electrode placement was performed between three and 13 weeks following autotransplantation, in the second between 33 and 41 weeks, and in the third group between 48 and 77 weeks.

In each case nine subserosal monopolar silver–silver chloride electrodes were sutured to the serosa of the intestine at the following sites: two electrodes were placed on the intact duodenum (ie, proximal to the autotransplanted segment) 5 and 25 cm from the pylorus; the remaining seven electrodes were sutured at equal distances along the length of the autotransplanted segment. Leads from each electrode came together in an abdominal cannula that was brought out onto the surface of the abdominal wall through a separate stab incision and sutured in place. This cannula served as the reference electrode.

All animals were weighed weekly and records maintained of their general condition, oral intake, and stool frequency.

Myoelectrical Recordings

Recordings of small intestinal myoelectrical activity commenced two weeks following electrode placement...