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Research article

Correlation between slow-wave myoelectric signals and mechanical contractions in the gastrointestinal tract: Advanced electromyographic method in rats

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ABSTRACT

Aim: Gastrointestinal motility disorders are presumed to be associated with abnormalities of the generation of slow-wave electric impulses. A requirement for the development of non-invasive clinical methods for the diagnosis of motility disorders is the identification of these signals. We set out to separate and characterize the signals from the various sections of the gastrointestinal tract and to detect changes in the smooth muscle electromyography (SEMG) signals.
Methods: Partially resected (stomach–small intestine, stomach–large intestine or small and large intestine) or non-resected male SPRD rats were measured under deep anaesthesia. Bipolar thread and disk electrodes and strain gauge sensors were used for SEMG and the detection of mechanical contractions, respectively. The electric activity was characterized by cycle per minute (cpm) and power spectrum density maximum (PsD_{max}) W by fast Fourier transformation analysis. Contractions were evaluated by area under the curve analysis.
Results: The myoelectric signals of the stomach, ileum and caecum were at 3–5, 20–25 and 1–3 cpm, respectively. Neostigmine increased (40–60%), while atropine decreased (30–50%) the PsD_{max} values. However, the cpm values remained unchanged. Linear regression revealed a good correlation between the PsD_{max} values and the smooth muscle contractions.
Conclusions: Electric signals of the same character were recorded from the organ and from the abdominal surface. The change in PsD_{max} perfectly reflects the change in the contractions of the smooth muscle. These results may serve as the basis for non-invasive gastrointestinal measurements in experimental animals, which can be translated into clinical practice for motility studies.

1. Introduction

Gastrointestinal (GI) motility disorders are among the unsolved clinical challenges. The most frequent forms of GI motility problems are oesophageal reflux disease, gastroparesis, ileus, and colon obstruction in intensive care (Aderinto-Adike and Quigley, 2014), but the daily clinical practice is additionally faced with gastric arrhythmia, heartburn, reflux, irritable bowel syndrome, chronic constipation, *etc.* (Varni et al., 2014). It is currently considered that these motility disorders are idiopathic in origin; their diagnosis, prognosis and treatment are therefore not satisfactory (Paine, McLaughlin, and Lal, 2013).

The GI smooth muscle has its own pacemaker cells, called the interstitial cells of Cajal (ICCs), which play a key role in the generation and propagation of the electric signal in GI contractility. ICCs generate slow-wave electric impulses to induce action potentials for contractions and determine the frequency of the signals (Lammers, 2015). Abnormalities in the function of the ICCs are presumed to be responsible for a number of GI disorders, including gastroparesis, chronic constipation and irritable bowel syndrome (Huizinga and Chen, 2014; O'Grady et al., 2014). Non-invasive GI electric mapping (multi-electrode method) and the electroenterogram (ring electrode method) as new techniques have been tested to characterize the GI motility, and especially the gastric activity in humans (Garcia-Casado, Zena-Gimenez, Prats-Boluda, and Ye-Lin, 2014; Yassi et al., 2012). Although these methods are promising, it cannot be guaranteed that the recorded signals originate solely from the putative GI tracts. The signals can obtain the GI slow- and fast-waves along with noises such as respiratory and motion artefact (Qin et al., 2015). The possibility of slow-wave myoelectric signal interference,

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or even masking with fast-wave signals from the brain, cardiac muscle or skeletal muscle, is very high, and an effort is made to reduce this through the special design of the sensors (Prats-Boluda, Garcia-Casado, Martinez-de-Juan, and Ye-Lin, 2011). Moreover, there are no unequivocal data as concerns the frequency parameters of specific myoelectric signals of the main segments (stomach, small and large intestine) of the GI tract. Identification of the signals from the various segments of the GI smooth muscle is therefore an essential requirement for the development of non-invasive clinical methods for the diagnosis of motility disorders of given parts of the GI tract. On the other hand, such a model may serve as an excellent method for smooth muscle pharmacology *in vivo*.

The aim of our study was to identify the slow-wave frequency parameters of the gastric, small intestine and large intestine segments of the GI tract. To attain this goal, we have developed a method with which to follow up the changes in myoelectric activity of the GI tract in parallel with the mechanical contractions in anaesthetized rats. The recording software has been equipped with effective electronic filters to separate the slow waves of the smooth muscle signals from the cardiac, brain and skeletal muscle activities.

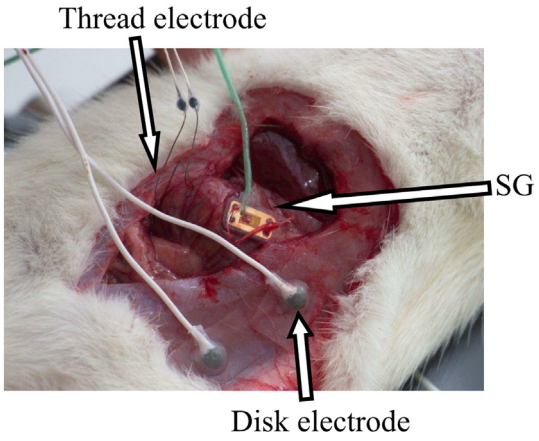

Fig. 1. Representative picture of the positioning of the electrodes and strain gauge (SG) for recording the caecal myoelectric and mechanical signals in a rat with a resected stomach and small intestine. The thread electrode pair and the SG were positioned on the caecum, while the disk electrode pair were positioned on the abdomen under deep anaesthesia.

2. Materials and methods

2.1. Housing and handling of the animals

The animals were treated in accordance with the European Communities Council Directives (86/609/ECC) and the Hungarian Act for the Protection of Animals in Research (Article 32 of Act XXVIII). All experiments involving animal subjects were carried out with the approval of the Hungarian Ethical Committee for Animal Research (registration number: IV/198/2013).

Sprague-Dawley rats (Charles-River Laboratories, Budapest, Hungary) were housed at 22 ± 3 °C and a relative humidity of 30–70%, under a 12 h light/12 h dark cycle. Standard rodent pellet food (Charles-River Laboratories, Budapest, Hungary) and tap water were provided *ad libitum*. Each animal was fasted for 2 h before the experiments.

2.2. Detection of gastrointestinal myoelectric activity

Male Sprague-Dawley rats (10–12 weeks old, body weight: 260–300 g) were anaesthetized intraperitoneally (i.p.) with a combination of ketamine and xylazine solution (36 and 4 mg/kg, respectively). The jugular vein was cannulated for later intravenous (i.v.) drug administration.

After laparotomy, the total GI tract was resected with the exception of one segment (stomach, small intestine or large intestine, n = 6 for each group) from the abdomen under deep anaesthesia. A bipolar thread electrode pair (SEN-15-1; MDE GmbH, Walldorf, Germany) was inserted into the serosal surface of the target organ (the distance between the two electrodes was 8 mm), while a bipolar disk electrode pair (SEN-15-2; MDE GmbH, Walldorf, Germany) was placed subcutaneously above the specific segment of the GI tract (the distance between the two electrodes was 20 mm). An implantable strain gauge (SEN-04-FSG2; MDE GmbH, Walldorf, Germany) was sutured onto the surface of the stomach, ileum or caecum, along the long axis of the muscle fibres, in order to detect the mechanical contractions (Fig. 1). So as to cover the incision, the surfaces of the abdominal wall were constricted and the abdominal skin was replaced after the positioning of the sensors. The animals were then placed immediately onto a heatable operating table (EXP-D-TC/MA-02; MDE GmbH, Walldorf, Germany) in order to maintain the body temperature (set to 37 °C). The basal activity was detected for 60 min. The electric signals were recorded and analysed by an on-line computer and amplifier system by the S.P.E.L. Advanced ISOSYS Data Acquisition System (MDE GmbH, Walldorf, Germany). Electromyographic (EMG) signals were amplified by using a custom-made amplifier designed by MDE Ltd., Budapest, Hungary. In order to reduce the artefacts we used a double-filter system. All analogue signals were pre-filtered with a first-order Bessel-type lowpass filter and were converted to digital signals at a sample rate of 2 Hz with a slope of 80 dB/decade. The pre-filtered myoelectric signals were then filtered further by Bessel-type bandpass filters with a frequency of 0–30 cycles per minute with a slope of 140 dB/decade. Each filter was a digital IIR filter. The recorded signals were analysed by fast Fourier transformation (FFT). The frequency of the electric activity was characterized in cpm, and the magnitude of the activity was described as power spectrum density (PsD). When more than one peak was found in the spectrum, only the highest peak was considered.

The mechanical contractions were evaluated by area under the curve (AUC) analysis of the primary contractility curves. Before the pharmacological studies, both the mechanical (strain gauge) and electric (thread and disk electrodes) signals were recorded for 30 min (n = 8 for each segment).

In the case of anaesthetized, non-GI tract-resected rats (n = 9), a bipolar disk electrode was placed under the abdominal skin, 1 cm right from the midline of the laparotomy, and 3 strain gauges were sutured one by one onto the surface of the stomach, ileum and caecum (Fig. 2). The abdominal incision surfaces were closed by surgical staples after the placement of the sensors. Both the mechanical (strain gauges) and electric signals (disk electrode) were recorded for 30 min before the administration of the investigated drugs. The myoelectric signals were

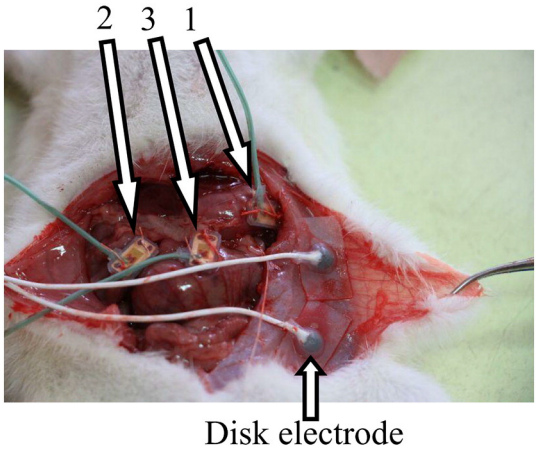

Fig. 2. The positioning of the disk electrode and strain gauges (1: stomach; 2: ileum; 3: caecum) for recording of the gastrointestinal (GI) myoelectric and mechanical signals in a non-GI tract-resected rat under deep anaesthesia.