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Electrical stimulation with motility analysis of five parts of the gastrointestinal tract

First evaluation of an experimental protocol in a porcine model

Abstract: Gastrointestinal (GI) motility disorders are frequent and clinically significant conditions with impairment of patient's quality of life. Examples range from upper GI symptoms such as dysphagia and gastroparesis to lower GI manifestations, namely chronic-intestinal pseudo obstruction, diarrhea and constipation. Furthermore, postoperative motility disorders are common. Currently, available pharmacological or dietetic treatment options are limited. Since GI motility is based on myoelectric activity, electrical stimulation (ES) is a promising alternative. Numerous studies have demonstrated suitable pacing strategies and parameters in different GI segments. However, results of multilocular ES are rare. We report the first experimental study to evaluate ES of five GI parts in a porcine model. Multi-channel electromyography (EMG) recordings of gastrointestinal baseline and poststimulatory electrical activity were realized together with video-based marker tracking (VBMT). ES provoked visible GI contractions and appeared to modulate frequencies of slow waves and spikes. Further investigations are needed for analysis of locoregional and cross-organ effects of ES on the GI tract.

Keywords: Gastrointestinal motility, Motility disorders, Electromyography, Video analysis, Electrical stimulation.

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https://doi.org/10.1515/cdbme-2018-0003

1 Introduction

Gastrointestinal (GI) motility disorders are common and clinically significant conditions with impairment of patient's quality of life. Functional upper GI manifestations include dysphagia and gastroparesis, while lower GI symptoms are chronic intestinal pseudo obstruction (CIPO), irritable bowel syndrome, diarrhea, fecal incontinence and colonic inertia with constipation. Furthermore, motility is impaired after any type of abdominal surgical procedure [1] resulting in postoperative gastrointestinal dysmotility or low anterior resection syndrome (LARS) with stool incontinence, urgency of stools and numerous bowel movements. However, a variety of poorly characterized syndromes remain subsumed as functional gastrointestinal disease (FGID) [2]. Symptoms of GI motility disorders are related to impaired electrical activity with motor disturbances during the interdigestive and postprandial state [3-5]. Since long term pharmacological or dietetic treatment is limited, electrical stimulation (ES) is a promising alternative. Numerous human studies have shown feasibility and promising results of single location ES of the stomach, small intestine and colon [4, 6].
In this study we tested the feasibility and safety of our experimental protocol for multilocular ES of stomach (GES), duodenum (DES), jejunum (JES), ileum (IES) and colon (CES) with assessment of electrical and mechanical activity by electromyography (EMG) and video-based marker tracking (VBMT) in a porcine model.

2 Material and methods

2.1 Animals and perioperative management

Six consecutive healthy male piétrain pigs with a median body weight (bw) of 30.5 kg (range: 26-36 kg) were investigated. Animal care and experimental procedures were approved by the ethics committee (see author statement). Animals were studied after an overnight fast under general anesthesia. All pigs were preanaesthetized with Azaperone (2-3 mg/ kg bw) before general anesthesia was induced and maintained with Thiopental Sodium (8-10 mg/ kg bw/ hour) and Piritramid (0.3-0.4 mg/ kg bw/ hour) adapted to heart rate and blood pressure. After intubation, ventilation was performed. Respiratory homeostasis, arterial blood pressure, electrocardiogram and body core and extraluminal gut surface temperature were monitored continuously. For minimization of cooling a thermal mattress and infrared lamp were used. Fluid loss was balanced by intravenous administration of Ringer's solution. Eventually, the animals were sacrificed with i.v. injection of 20 ml KCl 7,45 %.

2.3 Surgical procedure

After midline laparotomy a suprapubic catheter was inserted through the apex of the urinary bladder. Subsequently, stomach, duodenum, jejunum, ileum and colon were successively exposed under preservation of innervation and blood supply. Serosa was kept moist. Eleven bipolar hooked-wire electrodes and twenty-two monopolar hook needle pair electrodes were subserosally applied. Electrical stimulation was applied through seven additional monopolar hook needle pair electrodes. Two neutral electrodes were placed in the abdominal wall (inomed Medizintechnik GmbH, Emmendingen, Germany). Optical markers were attached on the visible gastrointestinal serosal surfaces and recorded on video with high resolution for VBMT (**Figure 1**).

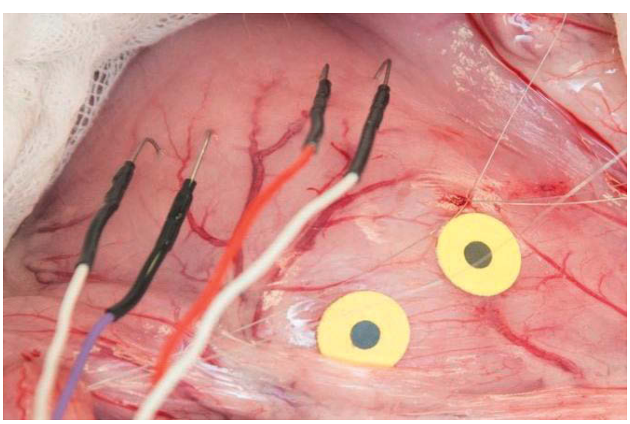

Figure 1: Pairs of hook needle and hooked-wire electrodes with optical markers on the serosal surface of the stomach.

2.4 Intestinal EMG signals and direct gastrointestinal electric stimulation

Multi-channel recordings of EMG signals and electrical stimulations were conducted with a computer and monitoring support system (inomed Xpress, inomed Medizintechnik GmbH, Emmendingen, Germany). All electrodes were evaluated by impedance measurements. Three minutes baseline multi-channel EMG was performed for all registered gastrointestinal spots before sequential GES, DES, JES, IES and CES. Electrical stimulation included four technical specifications and was sequentially applied. Every electrical stimulation setup was conducted twice according to the study protocol. After electrical stimulation three minutes EMG of all registered spots was completed (**Table 1**).

Table 1: Technical parameters of electrical stimulation

N	I [mA]	F [Hz]	PW [µs]	D-ES [s]	D-EMG [min]
1	25	30	500	30	3 + 3
2	25	130	500	30	3 + 3
3	25	30	1000	30	3 + 3
4	25	130	1000	30	3 + 3

Abbreviations: N= Stimulation parameter number, I= Amperage, F= Frequency, PW= Pulse width, D-ES= Duration of ES, D-EMG= Duration of pre- and poststimulatory EMG recordings.

3 Results

There were no anesthesia-associated complications in all six pigs. Gastrointestinal filling status was appropriate after overnight fast. After laparotomy, hook needle and hooked-wire electrodes were safely placed without perforation, leakage or major bleeding. Impedance measurements were in adequate range under 10 kΩ, indicating accurate positioning in the smooth muscle layer. Simultaneous multilocular multi-channel recordings of gastrointestinal baseline electrical activity were realized in all six cases in the stomach, duodenum, jejunum, ileum and colon. Recordings from subserosally implanted hook needle and hooked-wire electrodes showed rhythmic slow waves with fairly constant wave forms. More rapid frequencies were detectable as spike bursts (**Figure 2**).

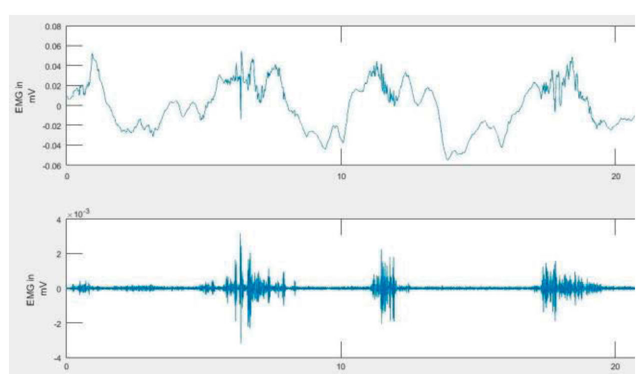

Figure 2: Electromyography analysis of the GI tract reveals rhythmic slow waves (upper image) and 30 Hz high-pass filtered spikes (lower image).

Electrical stimulation provoked visible contractions. After electrical stimulation the slow waves and spikes were still recordable and appeared to be frequency modulated. Simultaneous video recording and consecutive marker-based tracking revealed displacement of markers during contraction. An interaction between electrical activity and peak marker displacement could be found (**Figure 3**).

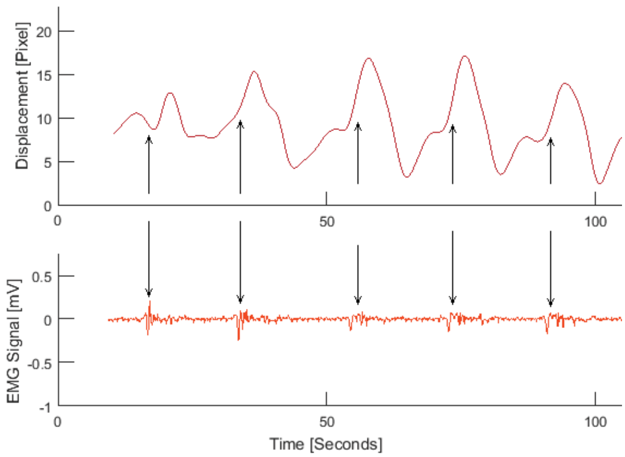

Figure 3: Simultaneous analysis of EMG recordings and VBMT reveals interconnection between EMG activity and pixel displacement (shown as signal samples of the stomach).

4 Discussion

This experimental study demonstrated the feasibility and safety of our experimental protocol for multilocular electrical stimulation of five different parts of the gastrointestinal tract in a porcine model with assessment of GI activity by EMG and VBMT. Until now, only a few studies were published with multilocular approaches. A chronic canine study analyzed the effects of GES, DES and CES on slow wave activity, but found effective pacing in the stomach and duodenum only [7]. Furthermore, Xu et al. triggered inhibition of gastric tone through four stimulation sites, namely GES, DES, IES and CES in dogs [8]. A single retrospective study investigated dual-device treatment with GES and sacral ES in fifty-four patients. Improvements of upper GI, lower GI and genitourinary symptoms as well as quality of life, assessed through questionnaires, were reported [9].

Both sequential and simultaneous ES of multiple GI locations may be performed with our utilized technical setup. To the best of our knowledge no previous study has shown feasibility of fivefold ES of the GI tract with analysis of electrical and mechanical activity. Further analysis of locoregional and cross-organ effects of ES on the GI tract is needed. Still, for upcoming investigations and first implantations of interactive microimplants, minimal invasive strategies will be evaluated.

Author Statement

Research funding: The project was funded by the Federal Ministry of Education and Research (BMBF, grant no. 16SV7638). Conflict of interest: Authors state no conflict of interest. Informed consent: Informed consent is not applicable. Ethical approval: The research complied with all the relevant national regulations and institutional policies for the care and use of animals and was approved by the Regional Board of Animal Welfare, Koblenz, Rhineland-Palatinate, Germany with approval code G-17-1-052.

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