Effect of subthreshold stimulation of vagal nerve on food intake pattern in swine

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Abstract

Aim. The aim of this study was to assess the usefulness of vagal nerve stimulation for controlling food intake in swine.

Methods. 21 adult Large White female pigs (15.42±2.43 kg) were used for this study. Food intake and body weight were monitored for 30 days, beginning 15 days before the performance of a laparoscopic surgery and for a further 15 postoperative days. Animals were randomly allocated to 3 groups, that underwent different laparoscopic procedures: ventral vagal trunk dissection (group C, n=5), non-functional stimulation implantation (group A, n=8) and functional stimulation implantation (group B, n=8).

One month (group A and C) or 15 days (group B) after surgery, blood samples were obtained from five animals of each group for systemic insulin and gastrin determination. Food intake and body weight recording were studied by COANOVA test or ANOVA test, respectively, and hormonal concentration values were analysed by Mann Whitney U test. A value of P < 0.05 was considered statistically significant.

Results. Despite causing no modification in food intake pattern in this study, vagal nerve stimulation caused changes in systemic gastrin and insulin concentrations. Vagal nerve stimulation increased basal plasmatic insulin and decreased postprandial response. Furthermore, an increase in gastrin was seen in group B throughout the study period.

Conclusions. Vagal nerve stimulation was not enough to provoke changes in short term ingestive behaviour in swine, but it did stimulate insulin and gastrin secretion.

1 Introduction

The only efficient treatment available nowadays for morbid obesity management is bariatric surgery. Despite their beneficial effect in decreasing body weight, these procedures are not exempt of complications, such as anemia, bone demineralization, stomach ulcer, etc. New techniques are being developed in an effort to avoid these complications, including gastric stimulation via an implanted subserosal bipolar lead [1] or vagal nerve stimulation [2]. Vagal nerve stimulation (VNS) has been used successfully in the treatment of epilepsy for several years. The benefit of VNS in patients with medically intractable complex partial seizures has been well documented [3].

In our previous experience we have demonstrated that vagal nerve stimulation reduces food intake in rabbits, that reduce solids ingestion to a 87% of preoperative values after VNS [4]. The present study was undertaken to assess whether these results could be reproduced in swine. In this communication, the results of food intake recording studies in pigs subjected to vagal nerve short-term electrical stimulation are reported.

2 Methods

The study protocol was conducted in compliance with the Guide for the Care and Use of Laboratory Animals, and it was approved by the Institutional Ethical Committee for Animal Research. Every effort was made to minimize the number of animals used.

Twenty-one Large White female pigs with an average body weight of 15.42±2.43 kg were used. This study comprised two phases. Firstly, the effect of vagal stimulation on food intake and body weigh was assessed. On the second stage of the study, changes on systemic gastrin and insulin concentration were studied. For the first phase, all animals were weighed weekly, always at the same time of morning and after a 19 hour-long fast. Pigs were daily offered food at the same hour (immediately after weighting when it was time to do so) and the amount of food consumed 5 hours after food administration was registered. Food intake
recordings were grouped in three preoperative and two postoperative intervals (in the early postoperative period food intake was not recorded) of 5 days each. Animals were randomly allocated to 3 groups, that underwent different laparoscopic procedures. Group C comprised 5 animals, and Groups A and B 8 animals each. The first group was sham operated (laparoscopic ventral vagal trunk dissection was performed) and served as control, Group A was subjected to laparoscopic non-functional stimulator implantation and Group B to a laparoscopic functional stimulator implantation.

The stimulators implanted in groups A and B were identical, but the one in group A was not activated. The device consisted of an impulse generator, which was placed in a serosal pocket created on the gastric surface and leads which were carefully attached to the ventral vagal trunk with a plastic cylinder. In group B, the vagal nerve stimulator delivered stimulation on a continuous basis all through the postoperative period.

Data were expressed as mean±S.D. Food intake and body weight recordings were analyzed by COANOVA test or ANOVA test, respectively, and hormonal concentrations were studied using Mann Whitney U test. A value of $P < 0.05$ was considered statistically significant.

<table>
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<th>Group A</th>
<th>Group B</th>
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</table>

Time points. (T0) basal, (T1) immediately before food administration, (T2) when the animal stopped eating, (T3) 15 minutes after T2, (T3) 30 minutes after T2 and (T5) 1 hour after T2.

**Table 1:** Systemic insulin (mU/l) concentration in each group.

<table>
<thead>
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<th>Tiempos</th>
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<th>Group B</th>
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<td>22.58±19.77</td>
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</table>

Time points. (T0) basal, (T1) immediately before food administration, (T2) when the animal stopped eating, (T3) 15 minutes after T2, (T3) 30 minutes after T2 and (T5) 1 hour after T2.

**Table 2:** Systemic gastrin (pmol/l) concentration in each group.
3 Results

All the animals survived the surgical procedure. No adverse effect attributable to the research protocol was observed during this study. No signs of discomfort were noted after the implantation of electroestimulation. There were no episodes of vomiting in any animal after stimulator implantation.

Food intake (p=0.001) and body weight (p=0.001) increased significantly during all the studied period.

Despite no significant changes in hormones concentrations having been evidenced in this study, the following trends were considered noteworthy:

Basal insulin values were higher in group B than in any other group (group C: 2.24±1.87, group A: 0.78±1.22 and group B: 5.58±4.77).

On the other hand, systemic insulin measured immediately after food administration was highest in group A, whereas during the postprandial period (T3 to T5), these values were greater in the control group (table 1). Regarding the maximum peak of insulin concentration, groups A and B showed a left deviation when compared to the control group, exhibiting similar values in T3.

Gastrin values were higher in group B in all the studied intervals (table 2). Lowest gastrin concentrations were seen in Group C at T0, T1, T3 and T4 and in Group B at T2 and T5. The maximum concentration peak, contrary to the insulin one, showed a right deviation in Groups A and B.

4 Discussion and conclusions

Despite stimulation parameters being the same that we have applied with good results in a previous study performed in rabbits [4], results were different in swine. These differences may be due, in our opinion, to the bigger size of the porcine ventral vagal trunk. Taking into account that the electrical impulses applied to the vagal nerve were constant in voltage, the intensity of the impulses varies according to the nerve diameter (according to Ohms Law) in both species. This may result in different fibers performing different functions being stimulated in each species. Andrew et al reported that stimulation subthreshold is lower in fast conducting fibers than in slow ones [5].

Vagal nerve stimulation with the parameters that provoke a decrease in body weight and food intake in rabbits were subthreshold for changing food intake pattern in pigs. However, these parameters increased systemic gastrin and insulin. This finding has been previously reported by different authors. In the study by Ahren et al [6] a vagal stimulation with 13.5 mA, 10Hz, 5msec, 10 min parameters stimulated insulin secretions in dogs. Similarly, Olesen et al [7] and Holst et al [8] reported that vagal stimulation increases gastrin concentration.

In conclusion, vagal nerve stimulation using parameters that have been proved useful to reduce food intake in rabbits was not enough to provoke changes in short term ingestive behaviour in swine, but it did stimulate insulin and gastrin secretions.

References


Acknowledgements

This study was partially supported by the Junta de Extremadura (Extremadura Regional Government of Spain). Ref.- IPR00B020.