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**The role of the vagal innervation of the stomach
(abomasum and pylorus) and intestine (duodenum) in
insulin and oxytocin release in sheep**

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ABSTRACT

Although mechanisms regulating nutrient partitioning and milk synthesis are not fully understood in ruminants, recent studies in lactating monogastric animals have shown that the vagus nerve modulates secretion of various hormones that are implicated in the short- and long-term control of nutrient partitioning. Therefore, the overall aim of this study was to examine the role of the vagal innervation of the GI tract on insulin and oxytocin release and milk yield in sheep. In a series of experiments described in this thesis, the effect of vagotomy was studied in ewes and wethers by comparing the responses of vagotomized animals (i.e. abomasal, pyloric, duodenal and hepatic branches sectioned) with control (sham-operated) animals.

Insulin release in response to a bolus injection of glucose was studied in lactating ewes (Chapters 2 and 4) or wethers (Chapters 3 and 5). The differences in responses were not significant in the experiments described in Chapters 3 and 4. However, the release of insulin from the pancreas in response to glucose injection was significantly ($P < 0.05$) suppressed in the vagotomized animals used in the experiments described in Chapters 2 and 5. Moreover in the experiments with wethers (Chapter 5), insulin secretion in response to glucose bolus injection was significantly ($P < 0.05$) higher when administered 2 h (i.e. fed state) following feeding than 22 h (i.e. fasting state). In addition, postprandial insulin concentrations were significantly ($P < 0.05$) lower in the vagotomized wethers than in the sham-operated wethers, but insulin secretion in the vagotomized wethers was apparently unaffected by plane of nutrition, despite significantly ($P < 0.05$) higher blood glucose levels in wethers on the HP intake. The insulin concentrations were, however, higher ($P < 0.05$) in the control group of wethers fed on the high plane (HP) of nutrition than those fed on the low plane (LP) of nutrition (Chapter 5).

Insulin was released in response to the sight and/or ingestion of food, cephalic phase insulin release (CPIR), without any significant changes in blood glucose concentrations. However, the increase in insulin concentration was significantly ($P <$

0.05) suppressed in both vagotomized wethers and ewes in comparison with control animals (Chapters 5 and 6).

Suckling increased plasma insulin concentrations in the sham-operated ewes but not in the vagotomized ewes (Chapter 6), although the difference in the concentrations between the two groups was not statistically significant ($P < 0.09$).

Milk and fat yields were significantly ($P < 0.05$) reduced for one day and two days, respectively, in the vagotomized ewes compared with those of sham-operated controls, but was restored over the next 2-3 days (Chapter 2). Milk yield was not different between the two treatment groups in the second study (Chapter 4).

Suckling-associated plasma oxytocin concentrations were significantly ($P < 0.01$) lower in the vagotomized ewes than in the sham-operated control ewes, although the difference was not statistically significant when corrected for baseline values (Chapter 4). In the next experiment (Chapter 6), oxytocin concentrations between the two treatment groups of ewes were not significantly different. However, in this experiment, suckling caused a significant ($P < 0.05$) increase in oxytocin concentrations from the baseline values in the sham-operated ewes fed and suckled simultaneously but not in the vagotomized ewes fed and suckled simultaneously.

Vagotomy significantly ($P < 0.05$) increased digestibility of dry matter and nitrogen in wethers, although food intake was not different between the two treatment groups (Chapter 3).

In conclusion, the findings in wethers (Chapter 5) agree with those in lactating ewes (Chapters 2 and 4) and, indicated that the effect of vagotomy on insulin release in response to glucose injection is more apparent over a short period (i.e. 2-4 h; Chapters 2 and 5) following feeding than after a longer period (i.e. 6-22 h; Chapters 4 and 5). This suggested that the pancreatic β -cells are more sensitive soon after feeding, because the vagal inputs reaching the β -cells from the GI tract are higher due to the recent consumption of food. The finding that post-prandial insulin concentrations in the

vagotomized animals of HP group were significantly reduced, despite their significantly higher blood glucose levels, provide further evidence that the vagus nerve is a major determinant for sensitizing pancreatic β -cells. Furthermore the vagal innervation of the GI tract plays a major role in C_{PIR}, and also appears to play an important role in insulin release during suckling in sheep. The concentrations of oxytocin measured in these experiments suggest that vagotomy interferes with oxytocin secretion although differences between vagotomized and sham operated ewes were often non significant. However, the data suggest that feeding stimulates OT secretion. It is possible that the failure to achieve consistent differences in milk ejection and hence removal in these studies may have been partly masked because of the anatomical features of the mammary gland of the ewe. Finally the activity of the vagus nerve influences the digestibility of dry matter and nitrogen in sheep.

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LIST OF ABBREVIATIONS

ADV	Abomasal and duodenal vagotomy
ANOVA	Analysis of variance
ATP	Adenosine triphosphate
BL	Balance
bw	Body weight
CB 154	2-Br-Ergocriptine
CCK	Cholecystokinin
CNS	Central nervous system
CPIR	Cephalic phase insulin release
CT-HRP	Cholera toxin horseradish peroxidase
DM	Dry matter
DMH	Dorsomedial hypothalamus
DMN	Dorsal motor nucleus
EDTA	Ethylenediaminetetraacetic acid
g	Gram
GH	Growth hormone
GHRH	Growth hormone releasing hormone
GI	Gastrointestinal
GLP-1	Glucagon-like peptide-1
h	Hour(s)
HADV	Hepatic, abomasal and duodenal vagotomy
HP	High plane of nutrition
ID	Internal diameter
i.c.v.	Intracerebrovascular
i.m.	Intramuscular
i.p.	Intraportal
i.v.	Intravenous
K	The glucose clearance constant
kg	Kilogram
LP	Low plane of nutrition

ME	Metabolizable energy
min	Minutes
MJ	Megajoules
mmol	Millimole
MSG	Monosodium glutamate
N	Nitrogen
NEFA	Non-esterified fatty acids
ng	Nanogram
NTS	Nucleus tractus solitarius
OD	Outer diameter
OT	Oxytocin
PF	Post-feeding
pg	Picogram
PO	Post-operation
PRL	Prolactin
PVN	Paraventricular nucleus
RIA	Radioimmunoassay
s.c.	Subcutaneous
sec	Seconds
SO	Sham-operation
SON	Supra optic nucleus
SS	Somatostatin
VFA	Volatile fatty acids
VIP	Vasoactive intestinal polypeptide
VMH	Ventromedial Hypothalamus

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