Chapter 19
Feed intake and energy supply – growing pigs

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This chapter deals with:

- Important general principles of feed intake regulation
- Sensory factors
- Physical and metabolic regulation of feed intake
- Important hormones, paracrine factors and energy sensing systems and how they are regulated
- Principles of diet selection
- Anti-nutritional factors
- Influence of environmental factors and animal health status
- Models to predict feed intake

1. Introduction

Appetite in animals is expressed by their feed consumption, which is basically a function of their nutrient and energy requirements. The energy demands of growing pigs comprise the requirements for maintenance and for lean tissue and fat accretion. This implies that the requirements change over the growth period, and that pigs of different genotypes and with different capacity for lean tissue growth will have different demands. Appetite is driven by a positive feedback as the demands for energy increase. The maintenance requirement of a diet with an energy concentration of 14 MJ digestible energy (DE) per kg has been estimated to $0.03W^{0.75}$ where W is the body weight in kg, whereas the demand for animals in rapid growth of lean and fat tissue may reach four times the maintenance requirement, i.e. $0.12W^{0.75}$. If these values are applied to a 50 kg pig, its maintenance requirement would be covered by approximately 0.6 FUgp, whereas its requirement for rapid growth would be sustained by 2.5 FUgp. The corresponding values for a 100 kg pig would then be 1.0 FUgp for maintenance and 4.1 FUgp for rapid growth [8].

Over the last couple of decades, genetic selection of pigs has lead to a substantial increase in capacity for lean tissue growth. Simultaneously, the rate of fat deposition has been reduced, and the capacity for feed intake has declined: during the early 1980s voluntary feed intake (VFI) declined by 30 g/day annually, but this trend stabilized around 1990, and since then VFI has remained fairly constant while lean tissue growth has continued to increase by 4 g/day annually. The capacity for rapid lean tissue growth calls for a high VFI, whereas efficient feed utilization and limited fat

deposition requires a low VFI. Selection for efficient lean tissue growth seems to reduce fat deposition via a decline in intake, meaning that the main driving force for lean and fat deposition is VFI. Another view predicted that VFI is made up by an animal's intrinsic maintenance requirements and its inherent desire to retain body protein and fat. The animal's genetic drive to fulfil these goals would then make it consume the required amounts of nutrients and energy. The decrease in VFI was, according to this concept, caused by pigs being selected for lower fat deposition having lower energy requirements. Previously, pigs were generally fed restrictedly in order to avoid excess fat deposition, but genetic improvement in the capacity for lean tissue growth has lead to lower feed intake (appetite), and feed intake capacity may in some situations be limiting for animal performance. Regulation of feed intake is a very complex process involving integrated systems, and with considerable redundancy. The knowledge on how feed intake is regulated has increased considerably over the last years, but still the knowledge in some areas is incomplete. The aim of this chapter is to give a general overview of feed intake regulation, with specific focus on growing pigs, and to describe how VFI is affected by environmental factors [7].

2. General aspects on feed intake regulation

An animal's requirements for energy and specific nutrients are supposed to be met by intake of a sufficient amount of feed, and the intake ought to be regulated so as to prevent both under-eating and over-eating. The feed intake is regulated on a short-term basis, i.e. the initiation and cessation of separate meals, and on a long-term basis, i.e. the mature animal strives to maintain a constant body weight over a prolonged period of time. The physiology of regulation of feed intake has been studied for decades and it is still not completely understood. Early views of how the periphery interacted with the brain in regulation of feed intake were the glucostatic, lipostatic and aminostatic theories that proposed that circulating factors that reflected body fat stores/metabolic status acted as signals to the brain, resulting in changes in energy intake or expenditure. Current concepts recognise that body weight and energy intake in animals are regulated by complex homeostatic mechanisms involving interactions between peripheral organs (e.g. adipose tissue, gut, thyroid, muscle and gonads) and the central nervous system (CNS). Signals produced peripherally then inform brain centres on the nutritional and metabolic status of the animal. This information is received and integrated by the CNS, and energy intake and expenditure are adjusted accordingly.

The gastro-intestinal tract receives innervation from the parasympathetic (cholinergic) and from the sympathetic (noradrenergic) autonomic nervous systems. The parasympathetic system includes vagal and pelvic nerves, and the sympathetic system comprises splanchnic nerves. In addition, the gastro-intestinal tract also has its own nervous system, i.e. the enteric nervous system, which is involved in every aspect of gut function, from mastication to defecation. The enteric nervous system is also involved in gastric and pancreatic exocrine secretion, gut motility, blood supply and hormone release. The enteric nervous system projects to the CNS through vagal and sympathetic (spinal) nerves, projections that transmit information to several CNS areas, including mechanical stimuli (distension, contraction), chemical stimuli (presence of nutrients in the gut lumen) and neurohumoral stimuli (gut hormones, neurotransmitters and neuromodulators). Most of these afferent vagal fibres terminate in the nucleus of the solitary tract (NTS) in the brainstem. Some signals from the gut are transmitted from the NTS to higher neural centres, such as, for instance, the paraventricular (PVN) and arcuate (ARC) nuclei of the hypothalamus. The integration of all these afferent signals related to feed presence in the gut regulates the size of individual meals (review by [10]).

The main hypothalamic centre for feeding control is considered to be the ARC, in which the blood brain barrier (BBB) is modified so that peptides and proteins (e.g. leptin and insulin) from circulation are able to pass. Other brain centres that are central in the regulation of feed intake are the PVN, the ventromedial hypothalamic nucleus (VMH), previously looked upon as "the satiety centre", and the dorso-medial hypothalamus (DMH), which is considered an integrative centre in which information from other hypothalamic areas is processed [10].

3. Sensory factors and their impact on feed intake in pigs

Sensory factors are known to exert influence on feed intake, but their relative importance differs between animal species. Hence, the sight of feed induces salivation and expectation of feed intake in dogs, whereas it would be very impractical if the same sensations were imposed on a grazing animal when let out on pasture.

Vision influences feed intake in several ways. It is of importance in the process of learning to recognize a certain feedstuff or type of feed and, for animals being able to discriminate between colours, colour may be a strong cue for learned aversions and preferences. The pig, however, appears to have rather poor sight so vision is not likely to exert a major influence on VFI in pigs. Their colour perception is, compared to for instance birds, not well developed, and given the choice between feed troughs of different colour no effect on feed intake was recorded [13].

Taste may have a positive or a negative influence on VFI. Taste can inform the animal on content of nutrients in the feed, but also on the occurrence of harmful substances. Taste is therefore important in making animals select suitable feed items and to avoid harmful or even toxic substances. The five defined different tastes are sweet, umami, salty, sour and bitter. The sweet taste is mainly derived from sugars, but also some d-amino acids confer sweet taste. Umami relates to l-amino acids and oligopeptides, whereas salty and sour relate to salts, e.g. NaCl and acids, i.e. H^+ ions, respectively. Bitter taste is related to toxic or anti-nutritional compounds. Sweet, umami and salty tastes are largely experienced as pleasant, whereas sour taste is unpleasant and bitter taste unpleasant or even repulsive. Taste buds occur in the oral papillae, which mainly are located on the tongue, epiglottis and soft palate epitheliums. The taste buds contain taste cells that are stimulated through taste receptors, and porcine taste receptors for umami, sweet, bitter and salty tastes have been identified. Pigs show a preference for sweet taste, and early work showed significant increase in feed intake after inclusion of 3-5% sucrose in the diet. Sweet is also a preferred taste by the dog, but not by the cat, which by its diet is not particularly exposed to sugars [12], [6].

Olfactory inputs may facilitate the location of feed for an animal, and the olfactory system in the pig is extremely well developed. Its olfactory neuro-epithelium, which is located in the upper wall of the nasal cavity, covers a surface area of almost 300 cm^2 compared to only about 5 cm^2 in human subjects. An example of pigs' exceptional sense of smell is their ability to locate truffles growing underground. The sense of smell plays an important role already for the neonatal piglet that is able to discern the smell of its mother and, furthermore, shows preference for the odour of maternal faeces and skin secretions [12], [13].

Flavour may be used as a tool to improve feed intake in newly weaned piglets: experiments have been performed in which flavours were added to the sow gestation and lactation period diets with the expectation that the flavour would pass to the amniotic fluid and milk. When a certain flavour was added to the sow lactation diet and the same flavour was included later in the piglets' weaning diet, the feed intake of the piglets increased by 10-12% and the weight gain improved by 10% in one study and in another by 24% (450 vs. 363 g/d). This effect of vertical flavour transfer appeared to be most pronounced during the first two weeks post-weaning. Another study examined the effect of both pre- and post-natal exposure to flavour, and weaning to a flavoured diet or an unflavoured control. The results suggested that irrespective of post-natal treatment, piglets exposed to flavour prenatally ingested more feed the first few days after weaning than did unexposed piglets [3]. These findings could be important to developing strategies to minimize the post-weaning anorexia generally occurring in piglets.

As appears from above, the combined senses of smell and taste are critical to pigs' appraisal of feed, although it has been shown that pigs that were olfactory bulbectomized soon learnt to use exploration to locate feed. The expression palatability of a feed is often used, and though it is very difficult to give an adequate definition of what it includes, it may be looked upon as a measure of the overall sensory impression the animal gets of a certain feed, among which released odours can

be expected to play a major role. Since palatability ought to be considered in context with several other factors too, such as the experience and metabolic status of the animal, physical features of the feed, e.g. texture, particle size and water holding capacity, it is not easily measured. The palatability of a feed may therefore depend on the situation in which it is offered to the animal.

4. Control by feedback signals

An animal consuming discrete meals starts eating when feeling the sensation of hunger and it stops feeding when it feels satiated. That eating ceases is an effect of a combination of signals caused by the ingestion of food and monitored to the brain. They are usually a combination of physical and chemical/metabolic stimulation, and are, together with the routes by which the information reaches the brain, called negative feedback pathways. Receptors in different parts of the gastro-intestinal tract are to various extents involved in the feedback control. Receptors present in the mouth and throat are important from a sensory point of view, but they are not likely to play any role as negative feedback signals.

4.1. Physical factors

The anatomy of the digestive tract and the type of feed the main intake is derived from may be factors of importance to the regulation of feed intake. Limitations owing to the capacity of the gut are of importance for monogastrics, but seem to be less limiting for intake than for ruminants, partly because of less variation in energy density of diets fed to the most important domestic monogastrics. In pigs, the rate of emptying the stomach into duodenum seems to be an important signal in intake regulation. If feed is removed from the stomach at a faster rate than the normal outflow, it will cause the animal to eat for a longer period, and reversely if gastric emptying is slow the animal will terminate its meal earlier.

Distension of the stomach is a contributing factor in controlling feed intake, but it has been demonstrated with dogs that inflation of a balloon in the stomach, despite resulting in a decreased feed intake, did not stop the animals completely from eating. No such research has been reported for pigs, but mechano-receptors are present in the stomach wall and they will most likely contribute to limit intake by signalling a sensation of fullness. The physical limit for feed intake in pigs is yet unknown, but when a diet is diluted with indigestible material so that its energy density decreases, pigs are to a certain extent able to compensate by increasing their feed intake and thereby maintain a constant intake of metabolisable energy. However, this compensation does not occur instantly; it takes some days before the pigs reach their maximum intake, and once this maximum level is reached it takes a correspondingly long time to wind it down when the pig is offered a more concentrated diet. The pig is able to compensate for variation in energy density over a fairly wide range, but the compensation cannot be sustained indefinitely, and there comes a point beyond which the daily energy intake cannot be further increased. In a study where the dietary energy density ranged from about 10 to 14 MJ digestible energy (DE)/kg, corresponding to approximately 0.78 – 1.09 FUgp, this physical limit for intake was reached earlier in small (young) pigs than in larger (older) animals. Pigs in the weight interval 27 – 50 kg on the diet with the lowest energy concentration were unable to increase their intake to such an extent that they consumed similar amounts of energy as pigs on diets with higher energy concentration. For the largest pigs (95 – 118 kg) the energy intake was almost independent of dietary energy density. The small pigs also needed longer time to adjust their intake to dietary energy concentration than the large pigs that were capable of a faster adaptation. These findings suggest that physical regulation of feed intake is dominating in young pigs whereas older animals to a larger extent regulate their feed intake from metabolic signals.

Similar outcomes were obtained in a study with pigs from 12 to 25 kg live weight where a highly digestible control diet (B) (13.7 MJ DE/kg; approx.1.08 FUgp/kg) was diluted with wheat bran (W) to give the following diets:

- 75B25W (12.5 MJ DE/kg; approx. 1.0 FUgp/kg),
- 50B50W (11.2 MJ DE/kg; approx. 0.9 FUgp/kg),
- 25B75W (10.0 MJ DE/kg; approx. 0.8 FUgp/kg), and
- 100W (8.7 MJ DE/kg; approx. 0.7 FUgp/kg).

The pigs were able to compensate their intake so that the daily feed intake in kg was highest on the 50B50W diet, although the weight gain was poorer, probably caused by a lower energy intake. However, when calculated for the last part of the feeding period and scaled to intake per kg body weight, the pigs had adapted further and pigs on the 25B75W diet had the highest intake per kg body weight. When animals were switched from a more concentrated to a bulkier diet it was evident that pigs that had experienced bulky feed previously were able faster to compensate for the dietary dilution and were better capable of adjusting to the less concentrated diet. Approximately a two-week period was needed for the pigs to adjust to the more fibrous feed.

The water holding capacity (WHC) of a feed has been shown to be strongly determining for maximum feed intake capacity of pigs given bulky feeds. When replacing a basal diet (B; WHC by centrifugation 1.5 g/g) with diets comprising either 50% B+ 50% dried grass meal (G; WHC 3.4); 100% G (WHC 5.3); 50 % B + 50% dried citrus pulp (C; 3.9); or 100% C (WHC 6.6), the feed intake in g per kg body weight per day was linearly related to the reciprocal of the WHC of the diet, and the diets with the highest WHC also caused the highest gut fill. When WHC exceeded 4, the feed intake decreased by about 6 g per kg pig live weight per unit increase in WHC. Similarly, when feeding control (WHC 3.5), wheat bran-based (WHC 4.6) or sugar beet pulp-based (WHC 10.0) diets in a change-over design to pigs from about 14 kg live weight, the sugar beet pulp-based diet was limiting for feed intake and for animal performance. It was shown, though, that when animals switched from the diet based on wheat bran to the diet based on sugar beet pulp, they consumed more feed than controls did when they switched to the diet based on sugar beet pulp. When on the sugar beet pulp-based diet, the pigs spent more time visiting the feeder, but the feed intake rate (g feed/minute) was lower than on the other diets. These studies show that feedstuffs with high WHC, typically diets with a high content of soluble fibre, are very likely to be limiting for feed intake, especially in young pigs, and the energy consumption decreases. When bulky feeds are fed, water is retained in the gut throughout the passage of feed, possibly making stretch receptors signal that the capacity for gut fill is reached. The retention of water in the gut after consumption of bulky feeds with high WHC results in increased weight and water content of the faeces produced. Although some adaptation occurs over time, pigs are unable to increase the intake to a similar level of energy as for diets with lower WHC. Diets with high WHC will increase mastication time, and more saliva will be produced. It has been suggested that increased chewing time may be necessary for swallowing diets with high WHC, and that hence the rate of feed intake would decrease.

However, the inclusion rates of bulky feedstuffs in the experiments described above were extremely high, and such extreme diets are not likely to be used for growing pigs in practical feeding. Therefore, a review of the “Role of the intestine in regulation of food intake in growing pigs” concludes that “It seems likely that gastrointestinal distension is not normally a very important limiting factor in determining food intake in the growing pig. The pig is able to adjust its intake to compensate for quite wide variations in dietary energy concentrations, however there are physical limits, and eventually gastrointestinal fill limits intake.” Further, it is concluded that in very young pigs “gastric distension is a major satiety stimulus”. This may be exemplified by the estimates of Kyriazakis & Whittemore [8] stating that bulk effects may exert appetite restraints on young piglets at DE values below 20 MJ/kg (to be compared with values for sows’ milk around 30 MJ/kg), for young growers and lactating sows at 14 MJ/kg and for other adults at 10 MJ/kg. Another approach to estimate physical limits to feed intake is based on the output of organic dry matter in faeces of a pig, which is surmised to be approximately 0.013W, where W is animal body weight. The physical limit for

feed intake would then be (kg/day) ≈ 0.013W/(1 – digestibility coefficient). For a 100 kg pig consuming a diet with 80% digestibility this would mean that the physical limit for feed intake would be 0.013x 100/(1 – 0.8) = 6.5 kg/day. If a diet with a poor digestibility of 65% was fed then the physical limit for feed intake would be reduced to 3.7 kg/day.

4.2. Chemical and metabolic factors

Feedback signals from the intestine include information from stretch receptors, osmoreceptors or chemoreceptors, but the relative importance of these is not completely clear. For the pig it has been shown that there are specific glucoreceptors in duodenum, and it seems likely that they exert an influence on feed intake in combination with an osmotic sensitivity, which may be caused by stimulation of stretch receptors when water is drawn into the gut to dilute its hypertonic content.

In monogastric animals, blood glucose concentrations fluctuate as a response to feeding, and, when possible, the animal attempts to keep concentrations as constant as possible. Based on this, the glucostatic theory was proposed claiming that the animal strived to maintain the blood glucose concentration as stable as possible by a central nervous monitoring system. This theory has later been modified in several ways, but the concept is still that the animal, by feeding, attempts to maintain the supply of energy in the body at a rather constant level. Pigs are generally fed diets with a high content of starch, and glucose is therefore the most important product of digestion, and glucose as a satiety signal has been investigated in several studies, but results are conflicting and still the role of glucose in inducing satiety is unclear. Forbes [5] reviewed studies on effects of glucose, protein and fat infusion into the stomach and different parts of the small intestine of pigs. Regarding glucose it was concluded that although glucose infusion depressed feed intake in some studies, there is still uncertainty whether the effects were due to osmolality, to glucose sensitive receptors in the gut wall, or to post-absorptive effects, especially in the liver. The role of glucose as a satiety factor in practical feeding situations remains obscure, but if level blood glucose concentration or constant energy supply to the body are key factors, ad libitum feeding systems would be preferable.

The satiating effect of protein or protein hydrolysate infused into the stomach or different parts of the small intestine seems to be proportional to the amount of energy infused, although the effects have ranged from almost none to a reduction corresponding to the double energy content of the infusion. The effect may be mediated by intestinal receptors which respond only to amino acids, but this awaits confirmation in studies on pigs. Fat infusion may also cause depression of feed intake, and some evidence indicates that the effect is mediated by mono-glycerides, whereas other studies report that the degree of unsaturation of the fatty acid infused is determining for the response [5]. The practical importance of these findings remains to be elucidated.

The “ileal brake” concept was introduced in 1984 when it was demonstrated that infusion of a partially hydrolysed triglyceride solution into the ileum of humans markedly increased feed transit time. It has later been convincingly shown in several mammal species, including pigs, that the presence of nutrients, or their breakdown products, in the intestine has a negative impact on the rate of gastric emptying, propulsive peristaltic activity as well as the rate of gastric acid, pancreatic and bile secretion, resulting in reduced feed intake. Lipids seem to exert very potent ileal brake effects, and lipid-based compounds and fatty acids have been extensively investigated. The negative effect on feed transit time has been demonstrated to be related to the amount of lipid administered, the kind of lipid, and the site of infusion. Hence, the more lipid that was administered, the stronger was the ileal brake response. When effects of free fatty acids, triglycerides and glycerol were compared it was shown that glycerol did not at all activate the ileal brake, and it was convincingly demonstrated that presence of free fatty acids in the intestine was necessary to induce ileal brake effects. Regarding length of the carbon chain, it seems that medium chain triglycerides of 12 or fewer carbon atoms more rapidly induce ileal brake effects than longer chain triglycerides, possibly because of more rapid absorption of medium chain triglycerides, which are absorbed directly to the portal circulation without formation of chylomicrons. Furthermore, unsaturated fats evidently induce stronger ileal brake effects than saturated ones. Gastric emptying, digesta passage rate through

the intestine and intake of feed are more depressed when nutrients are present in the distal part of the tract (ileum and colon) than when in the more proximal parts of the tract, the effectiveness of the brake being greatest in colon, followed by ileum and least efficient in jejunum (review by [2]). Satiety induced by ileal brake effects is not very likely to occur in practical pig feeding, unless in situations when diets with an elevated fat content are used, e.g. for lactating sows.

The role of osmolality in the regulation of food intake is still an open question. When hyper-osmotic solutions have been infused into the duodenum of pigs, feed intake has been reduced, but when pigs are given free access to drinking water the osmolality of the duodenal fluid remains below 300 mOsm/kg, and even in an ad libitum feeding situation the maximum level of osmolality is maintained at slightly above 300 mOsm/kg. Intestinal receptors that are sensitive to osmolality are also sensitive to other stimuli, so osmotic effects may be a combined effect of osmolality and other stimulation of gastrointestinal receptors [5]. In practical pig production, when animals have water available at all times, it is not very likely that osmotic effects will be limiting for feed intake.

Absorbed glucose and amino acids are directed to the liver where they are further metabolised. The liver can therefore be potentially important in the regulation of feed intake. Studies in mono-gastric animals have demonstrated that infusion of oxidizable nutrients into the hepatic portal vein depresses feed intake, but infusion into the jugular vein has much less effect. On the other hand, blocking of the fatty acid oxidation has led to an increased feed intake in rats. Therefore, the supply of oxidizable nutrients to the liver seems to be an important control mechanism in the regulation of feeding, and there is evidence that it is the oxidation step as such that is important. However, there is still some doubt regarding the importance of the liver in feed intake control under physiological conditions. Studies with infusion of glucose and amino acids into the hepatic portal vein of pigs have, however, failed to affect feed intake, but pigs were fasted overnight and it was speculated that hunger might have outweighed the effects of glucose infusion [5].

5. Hormonal and paracrine control of food intake

Feed intake regulation is very complex, and a variety of hormones, neuropeptides, metabolites and signal substances are involved. The main route of communication between the brain and the gut in relation to energy homeostasis is via the circulation, and this section will give a general description of the role of the most important circulatory factors involved in feed intake regulation (Table 19.1). Data specifically concerning pigs is not available for all these factors, but, when possible, research concerning pigs will be used.

5.1. Gut hormones

When nutrients and metabolites arrive in the gastrointestinal tract (GIT) they stimulate the release of several peptides with regulatory function on gastric emptying, gastric acid secretion, intestinal motility and secretions from the pancreas and the gall bladder. Among them are cholecystokinin (CCK), bombesin, glucagon-like peptide-1 (GLP-1), peptide tyrosine tyrosine (peptide YY; PYY), and oxyntomodulin (OXM), which all have suppressive effect on feed intake, and ghrelin, which stimulates appetite. There are several others, which will not be addressed here, and the regulatory mechanisms are very complex.

Table 19.1. Examples of molecules with documented effect on feed intake in some animal models (modified after [10]).

Orexigenic: Feeding stimulators	Anorexigenic: Feeding inhibitors
Agouti-related peptide	Adiponectin
γ - Aminobutyric acid	Amylin
β - Endorphin	Bombesin
Corticosterone	Cocaine and amphetamine-regulated transcript
Dopamine	Cholecystokinin
Endocannabinoids	Corticotrophin-releasing hormone
Growth hormone	Glucagon-like peptide-1
Growth hormone releasing hormone	Insulin
Glutamate	Insulin-like growth factors I and II
Ghrelin	IL-1
Melanin-concentrating hormone	IL-6
Noradrenaline	Long chain fatty acids
Neuropeptide Y	Leptin
Orexins (A & B)	α - Melanocyte-stimulating hormone
Thyroid hormones (tri-iodothyronine)	Oxyntomodulin
	Pancreatic polypeptide
	Peptide YY_{3-36}
	Resistin
	Serotonin
	Thyrotrophin-releasing hormone
	Urocortin

One of the earliest discovered hormones with a well known role in appetite regulation is the gastro-intestinal hormone CCK, which is secreted in the duodenum and the jejunum into the blood circulation in response to nutrient ingestion (protein and fatty acids). In the early phase of its release it stimulates gastric emptying, pancreatic and gall bladder secretions and accelerates transit in the proximate intestine, i.e. stimulates further feed intake. In the distal GIT, however, release of CCK and gastrin stimulates release of three other peptides (PYY, GLP-1 and OXM) with suppressive effect on feed intake from the ileum and colon. This release occurs long before digesta has reached this part of the tract and it generates a feedback mechanism that results in slowing down of gastric emptying, and decreases the gastric acid as well as pancreatic and bile secretions. Further, it decreases proximal intestinal motility and it initiates meal cessation [2]. The information to the CNS to stop feeding is transmitted by CCK crossing the BBB and acting on neuropeptide Y (NPY) neurons (see below) [10]. Thus, CCK is the factor that initiates termination of a meal, but it acts in concert with other peptides.

The involvement of CCK in feed intake regulation in pigs has been demonstrated e.g. in two different lines of pigs, one selected for fast growth (F) and another selected for slow (S) growth. Barrows of these two lines were studied in two experiments in which feed consumption and plasma concentrations of CCK were recorded. In the first experiment, the pigs were allowed ad libitum access to feed. Plasma CCK concentrations increased significantly as feed consumption was initiated. Pigs from the S line consumed less feed than F pigs, and plasma CCK concentrations, averaged across samplings, tended to be higher in S than in F pigs (P=0.07). When CCK was expressed in relation to feed intake over the 2 hour-period that feed intake and CCK were recorded, the ratio was highest for S pigs at 10, 20 and 30 minutes, but similar among both lines 60, 90 and 120 minutes after introduction of feed. In a second experiment, the pigs were pair-fed to the same level as the consumption of the S pig in the ad libitum feeding situation, and feed intake and plasma CCK concentrations were recorded. In this study feed intake was similar among lines, but although the average plasma CCK across sampling times was numerically higher in S than F pigs differences were non-significant. Overall, the results of these studies indicate that appetite in the pigs selected for slow growth with a lower voluntary feed intake than pigs selected for fast growth was suppressed by a higher ratio between plasma CCK and feed intake during the first 30 minutes

after ingestion of feed had started. When the confounding effects of different feed intake between lines were removed, no significant differences between lines were recorded, although there was a tendency to higher plasma CCK in slow growing pigs. This indicates that higher concentrations of CCK early after feed ingestion started in the slow growing pigs have induced satiety more rapidly than in the fast growing line.

The preproglucagon gene, which is widely expressed in the gut, yields two important satiety peptides, namely *GLP-1* and *OXM*. Release of GLP-1 and OXM from the distal part of the GIT occurs in response to the presence of NEFA and carbohydrates in the gut. Both central and peripheral administration of the peptides inhibits feeding. *Peptide YY* is secreted post-prandially (after a meal) in the distal GIT, especially in the ileum, colon and rectum, and the rate of PYY secretion reflects energy intake. The anorexic effect of PYY may, similar to GLP-1, be partially mediated by an aversive response. *Bombesin* is another peptide with inhibitory effect on feed intake. It is widely distributed in the mammalian GIT. Plasma levels of bombesin increase markedly after feed intake, and both peripheral and central administration of bombesin is anorectic [10].

Ghrelin is a hormone mainly synthesised and secreted at the fundus of the stomach, but also in duodenum, ileum, caecum and colon, and in other tissues too. This hormone was initially identified as the endogenous ligand of the growth hormone secretagogue receptor (GHS-R), and it exerts a potent and specific growth hormone releasing activity in vitro and in vivo. Ghrelin also plays an important role in energy homeostasis. Ghrelin administration induces positive energy balance in rodents without markedly changing energy expenditure or locomotor activity. In many species, plasma levels of ghrelin reflect feed intake, they increase during fasting and immediately before meals, and fall after feed intake. These changes in ghrelin expression are directly modulated by energy intake and nutritional signals such as blood glucose and ingestion of fat or carbohydrate. For this reason, a physiological role of ghrelin in meal initiation has been proposed. In the CNS, the action of ghrelin on feeding is mainly exerted in areas where expression of other important appetite stimulating neuropeptides occur. Besides its role in regulating hunger in the post-prandial period, ghrelin also plays a role in monitoring energy and weight status: ghrelin can be used to monitor body lean status in animals [10], [2].

In newly weaned pigs, plasma ghrelin concentrations were studied in animals that were either fed or deprived of feed for 24 hours and then refed. In the feed deprived pigs, plasma concentrations of ghrelin declined during the first 12 hours of feed deprivation, and then increased to a level significantly above that of the fed control group at 24 hours. After refeeding, plasma ghrelin concentrations remained elevated until the end of the experiment after 30 hours. This experiment was followed by one in which pigs were feed deprived for 72 hours. The pattern of plasma ghrelin followed that of the previous experiment, with an initial decline until 12 hours and then an increase. Ghrelin concentrations in plasma remained significantly higher than those of the control group until 48 hours, and then declined reaching a value lower than that of the control group at 72 hours. It was concluded that the low levels of serum ghrelin observed at 72 hours may reflect the inability of ghrelin synthesizing cells in the stomach to produce sufficient ghrelin to maintain serum concentrations at a high level. Other studies with pigs have reported similar responses in plasma ghrelin concentrations to feed deprivation, but in prepuberal gilts it was found that plasma ghrelin concentrations increased throughout the feed deprivation period and were significantly elevated over basal concentrations at 72 hours, and then returned to basal levels within 6 hours of refeeding. Results from a recent study where pigs were fed ad libitum twice a day or once a day with a sham feeding at the same time as the first daily feeding in the twice-a-day feeding regimen, implied that plasma ghrelin concentrations were more related to energy balance of the pig than feeding regimen. Plasma ghrelin concentrations were reduced with ad libitum feeding and elevated in response to once daily feeding.

The plasma ghrelin secretory profile also showed distinct differences in response to the three feeding regimens. In the twice-a-day and once-a-day feeding regimens, but not in the ad libitum, plasma ghrelin increased over the 12-hour blood sampling period. This data suggest that both circulating ghrelin concentrations and its secretory profile are responsive to the amount of feed an animal consumes. Therefore, the type of feeding regimen an animal is exposed to may influence ghrelin secretion, which in turn reflects the energy status of the animal.

Exogenous administration of ghrelin has been studied as a means to stimulate feed intake and body growth in 18-day-old, newly weaned piglets. Piglets were studied for 8 days in order to record relative body gain, feed intake and hormonal profiles via an indwelling jugular catheter for 5 days subsequent to 3 daily injections with either human ghrelin or saline. The weight gain of the ghrelin treated pigs was higher than that of controls despite feed intake, though numerically higher, did not differ significantly between treatments. However, behavioural observations showed that more ghrelin treated pigs were eating during the observation period than did control pigs. The initial infusion of exogenous ghrelin increased serum ghrelin, GH, insulin, and cortisol concentrations, demonstrating that ghrelin has a stimulatory effect on GH secretion as well as insulin and cortisol. These observations provide evidence that ghrelin may positively influence weight gain and concomitantly increase GH, insulin, both being anabolic hormones, and cortisol secretion in weaned pigs. Exogenous ghrelin administration may induce a positive energy balance, and treated piglets were therefore less affected by weaning anorexia and negative energy balance. Elevated GH might have contributed to a higher rate of lean tissue accretion. Further support to the appetite stimulating effect of ghrelin in pigs was given by a study that found that pigs immunized against ghrelin at 19 weeks of age had more than 15% lower VFI and gained less weight than controls during days 10-55 after immunization. To conclude, ghrelin exerts a stimulating effect on feed intake, and the localisation of its expression in the CNS is found at similar sites as other neuropeptides that induce increased feed intake. By stimulating the secretion of GH and insulin, and by inducing positive energy balance, it exerts anabolic effects, and can therefore contribute to stimulate growth.

5.2. Adipose tissue hormones

For a long time, adipose tissue was looked upon as an inert energy storing tissue, but over the few last decades its role as a highly active endocrine organ with a fundamental impact on metabolic processes in the body has been revealed. Adipose tissue produces hormones that regulate appetite, glucose homeostasis, lipid metabolism, endocrine function, cardiovascular physiology, reproduction, immune function and development, and other bodily functions. In this section a brief overview of those involved in regulation of feed intake will be given. The text is mainly based on the review by López et al. [10], which is of general character, but when specific studies relevant to feed intake regulation in pigs are available they will be discussed.

Among the adipocyte hormones, the one that has most changed the concept of white adipose tissue as an inert tissue is *leptin*, the product of the ob (obese) gene. Leptin is expressed principally in adipocytes, but also at lower levels in the gastro-intestinal tract as well as in a plethora of other tissues in the body. Plasma leptin levels reflect both energy stores and acute energy balance. Circulating leptin levels are tightly correlated with adipose tissue mass, and feed restriction results in suppression of circulating leptin, which can be reversed by refeeding or insulin administration. Chronic peripheral administration reduces feeding, resulting in loss of fat mass and body weight. The leptin receptor has several isoforms (OB-Ra, OB-Rb, OB-Rc, OB-Re and OB-Rf) and OB-Rb mediates the action of leptin on feeding. Plasma leptin crosses the BBB, and OB-Rb is widely expressed in the hypothalamus, the LHA and the medial preoptic area as well as in feeding-modulating neurons in the brainstem. In the hypothalamic ARC, OB-Rb mRNA is expressed by two major neuronal groups: first neurons co-expressing the orexigenic neuropeptides NPY and agouti-related peptide (AgRP) and secondly in a distinct population of neurons co-expressing the anorexigenic pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART). Leptin inhibits the activity of appetite stimulating AgRP/NPY neurons and reduces expression of AgRP and NPY, while activating anorectic CART/POMC neurons. This results in decreased feed intake. In the LHA, leptin receptor is expressed in neurons expressing the orexigenic neuropeptides melanin-concentrating hormone (MCH) and orexin (OX), which are inhibited by leptin. When leptin

levels are low, such as in feed restriction and fasting, the expression of orexigenic neuropeptides is increased and orexigenic neurons are activated; in contrast, anorexigenic neuropeptides are decreased and anorexigenic neurons are inhibited. When plasma leptin levels are high, as in the satiated animal, the anorectic pathways are switched on and the orexigenic pathways are switched off.

The earliest studies in pigs showed that, similar to in other species, plasma leptin concentration and leptin gene expression reflect body fat mass, and, consequently, pigs with greater adipose tissue mass or selected for greater fat deposition have higher circulating leptin and leptin mRNA than pigs with greater lean tissue mass. The role of leptin in feed intake regulation in pigs was first demonstrated when intracerebro-ventricular (ICV) injections of 10, 50 and 100 µg recombinant porcine leptin resulted in reduction of feed intake by 53, 76 and 90% in the respective treatment groups 20 hours after injection.

However, the role of leptin in feed intake and body fat content regulation is far more complex, and possibly different in very young and older pigs. These differences may be caused by differences in body fat content or metabolism. Weight loss and feed restriction do not necessarily result in parallel changes in blood leptin and expression of its mRNA: in castrated male pigs fed ad libitum from 55 to 163 kg body weight, relative abundance of leptin mRNA correlated with fat mass and body fat per cent, and increased with increasing body weight. However, four weeks' feed restriction leading to considerable body weight loss did not change the relative abundance of leptin mRNA, whereas total feed deprivation for 3 days reduced the expression of leptin mRNA by more than 30 % in pigs weighing 60 and 136 kg. In newly weaned piglets exposed to 72 hours' feed deprivation, serum leptin concentrations were reduced below those of the animals fed 12 hours after feed removal, and after 72 hours feed deprivation adipose tissue leptin mRNA expression was decreased. When the animals were refed serum, leptin concentrations returned to the level of fed animals after 12 hours, but the relative abundance of leptin mRNA had not changed after the 24-hour refeeding period. The rapid decline and increase in serum leptin in these young pigs was unexpected, because such small pigs do not have large body fat reserves, and 72 hours' feed deprivation could have been expected to deplete the reserves to such an extent that it would take longer time to restore serum leptin concentrations. These studies demonstrate the complexity of leptin regulation, and that it is therefore difficult to estimate the quantitative importance of leptin in feed intake regulation of growing pigs.

Adiponectin is a 244-amino acid protein secreted from adipose tissue, the placenta and cardiomyocytes. Adiponectin is important in the regulation of energy homeostasis, and plasma levels of adiponectin are inversely correlated with adiposity. Circulating adiponectin level negatively correlates with insulin resistance, and treatment with adiponectin can reduce body weight gain, increase insulin sensitivity and decrease lipid levels in rodents. Adiponectin does not cross the BBB, making a direct effect of adiponectin in the CNS unlikely. Despite the important role of adiponectin in regulating energy homeostasis, direct effects on feed intake regulation are not evident. Other adipose tissue hormones with possible relevance to feed intake regulation, body adiposity and insulin resistance are resistin and IL-6, but presently there is no information available on the importance of these hormones to feed intake regulation in pigs.

5.3. Pancreatic hormones

Insulin is, besides its other functions in the body, also an adiposity signal. Plasma insulin concentrations correlate with peripheral insulin sensitivity, which in turn is linked to total body fat depots and fat distribution, visceral fat being a key determinant. Insulin secretion by the pancreas increases rapidly after a meal, exerting an anorectic effect via the CNS. Insulin enters the CNS via a saturable receptor-mediated transport across the BBB. Central administration of insulin reduces feeding and body weight in rodents and primates. Insulin receptors are widespread in the brain and occur in hypothalamic nuclei involved in feed intake regulation (ARC, DMH, and PVH). In the hypothalamus, the actions of insulin on feed intake and body weight are mediated by NPY and the melanocortin system. *Pancreatic polypeptide* (PP) belongs to the PP-fold family of peptides, which

also includes PYY and NPY. PP is mainly produced by peripheral cells of the islets of Langerhans, the exocrine pancreas and the distal GIT. Plasma PP concentrations increase proportionally to energy intake, and they appear to be inversely proportional to adiposity, with high levels in anorexic subjects and reduced levels in obese subjects. The anorectic effect of PP is partly exerted via regulation of hypothalamic neuropeptides (NPY and OX) and modulation of ghrelin expression [10]. The role of PP in the feed intake regulation in pigs has not been investigated.

5.4. Hypothalamic neuropeptides involved in regulation of feed intake

Neuropeptide Y (NPY) is a thirty-six-amino acid peptide belonging to the PP-fold family of peptides, which also includes PYY and PP. NPY is widely distributed in the CNS and is one of the most potent stimulators of feed intake; repeated third ventricle or PVH administration of NPY induces striking hyperphagia and obesity. Central administration of NPY also reduces brown fat thermogenesis, suppresses sympathetic nerve activity and inhibits the thyroid axis in order to reduce energy expenditure. NPY mRNA levels and NPY release in the ARC respond to changes in energy status, being increased after fasting and feed restriction and decreased after refeeding [10].

Also in pigs, NPY has been shown to stimulate feed intake. The first study reporting such effects demonstrated that lateral cerebral ventricular injection of NPY significantly stimulated feeding behavior in a dose-dependent way even in satiated pigs during 30 minutes following injection. More recently, the possible interactions between ICV injection of porcine NPY and human recombinant leptin on feed intake in growing pigs were evaluated in an experiment where pigs were offered feed ab libitum and observed for 44 hours. The experimental treatments were injection with NPY, combined NPY and leptin injection, leptin injection or saline injection. Four hours after injection cumulative feed intake was similar in saline and NPY injected pigs, whereas it was reduced in pigs given leptin or the combined NPY and leptin treatment. When intake was measured 20 hours after injection, pigs injected with NPY and NPY plus leptin had consumed more feed than pigs treated with saline or leptin, and that the two latter groups did not differ in cumulative intake. By the final measurement point 44 hours post-injection, the cumulative feed consumption of the pigs given the NPY treatment was greater than that of any other group, but the feed intake in the group treated with leptin plus NPY had declined and was similar to that of the control group treated with saline. Compared with the groups treated with saline and NPY, leptin treatment reduced intake at all measured time points. This study therefore clearly demonstrated the stimulatory effect of NPY on cumulative feed intake in growing pigs.

The *melanocortin neuropeptide system* comprises *α-melanocyte-stimulating hormone (α-MSH), pro-opiomelanocortin (POMC)* and *agouti-related peptide (AgRP)*. Melanocortins play a prominent role in regulation of feed intake. The central melanocortin system modulates energy homeostasis through the anorectic actions of α-MSH (a POMC cleavage product) and AgRP. The feeding-related effects of both α-MSH and AgRP are mediated via two receptors, which are widely expressed in the hypothalamus. Circulating hormones such as insulin, leptin, ghrelin, PYY, glucocorticoids and oestrogens act on melanocortin AgRP and POMC neurons, providing information on energy status from the periphery. Hypothalamic POMC mRNA expression is regulated by nutritional status, with low levels during fasting that return to normal after leptin treatment or refeeding. In contrast, AgRP mRNA expression is increased by fasting, but unlike NPY mRNA levels, which are decreased after refeeding, AgRP levels remain elevated [10].

We know very little of the effects of products of the melanocortin system on feed intake and weight gain in pigs. The expression of e.g. AgRP and POMC were studied in piglets 4 days after weaning. Piglets were grouped into large and small according to weaning weight, and allocated to different dietary treatments at weaning. After 4 days of dietary treatment it was found that the expression of the orexigenic AgRP was strongly correlated with that of the anorexigenic POMC, and that expression of AgRP mRNA was more abundant among large than small piglets.

The *orexins (OX; OX-A and OX-B)* are neuropeptides derived from the common precursor prepro-OX expressed in the LHA/perifornical area. Although OX expression in the brain is only

located in the LHA–perifornical area, OX receptors show a widespread distribution in the CNS, with high levels of abundance in some hypothalamic nuclei. Orexin receptors are also present in other tissues, e.g. the gut. Evidence that links OX to endocrine function and feed intake regulation has been presented: Central administration of OX to rats stimulates feeding via an NPY-dependent mechanism. The expression of prepro-OX is increased in fasting and restored to normal by leptin. It may be possible that visceral feeding-related signals regulate OX actions. Thus, stimuli acting as 'terminate-eating' signals, such as gastric distension and glucose concentrations in the portal vein, appear to be important in the regulation of OX [10].

Orexin has been used successfully to stimulate feed intake in weaned pigs: Piglets that were weaned at 16 ± 2 days of age when weighing 4.97 ± 0.20 kg were housed individually in order to monitor feed intake, and one week after weaning a total of 25 pigs were allocated either to a control (n=12) or an orexin treatment group (n=13). Pigs were given an intramuscular injection of sterile water or synthetic orexin-B (3 mg/kg) solution. Feed intake was monitored every second hour for 24 hours, and finally the cumulative intake was calculated. The orexin-treated pigs had the same general feed intake pattern as the control pigs, but at 12 hours post-injection they consumed approximately three times more feed than controls in what seemed to be an extra meal. The intake profiles indicated that at regular mealtime, the orexin-treated pigs consumed more feed over a longer time period than controls. The cumulative feed intake of orexin-treated pigs exceeded that of control pigs through 12-24 hours post-injection. The results of this study suggest that feed intake in young pigs may be stimulated by peripheral injection of orexin. More recently, it was demonstrated that there was a positive relationship between weaning weight of piglets and the expression of orexin mRNA. Despite the stimulatory effect of orexin on feed intake, no further investigations into this area seem to have been performed on pigs.

Cocaine- and amphetamine-regulated transcript (CART) is the third-most-abundant transcript in the hypothalamus. Feed deprivation decreases ARC expression of CART, while peripheral leptin treatment in ob/ob mice increases CART expression. Central administration of CART inhibits feeding, and CART-knockout mice display a predisposition to become obese on a high-fat diet, supporting the role of CART in the hypothalamic mechanism regulating feed intake [10].

5.5. Monitoring of metabolic status

Two major systems, *adenosine monophosphate-activated protein kinase (AMPK)* and mam*malian target of rapamycin (mTOR)*, which act both peripherally and centrally in the hypothalamus, monitor energy status and adiposity of animals, and provide control of long-term feed intake, energy metabolism, body composition and body weight. The role of these systems in the regulation of feed intake in pigs is not particularly well known, but the same general principles as investigated in other species are likely to pertain.

AMPK responds to changes in energy status of cells and the whole body in order to make sufficient amounts of ATP available for essential metabolic pathways. AMPK is activated when lack of nutrients or oxygen supply, or excessive use of ATP such as during cold exposure and hard exercise, causes ATP to decline and AMP to rise. When AMPK is activated, ATP-consuming pathways, such as gluconeogenesis and fatty acid synthesis, are inhibited whereas pathways that produce ATP, i.e. glycolysis and fatty acid oxidation are stimulated. When an animal is in high-energy status the AMP:ATP ratio is low, and the activation of AMPK is low, and synthesis of fatty acids can occur. In this process, glucose is first converted to acetyl – CoA, which in turn is converted to malonyl – CoA. Malonyl – CoA together with bloodborne fatty acids in the form of fatty acyl – CoA are then converted to longer chain fatty acids to be stored in adipose tissue. As a consequence of this process the concentration of malonyl – CoA increases. When, on the other hand, the energy status of an animal is low, the AMP: ATP ratio is high as is the activation of AMPK, while the concentration of malonyl – CoA is low. This results in increased oxidation of fatty acyl – CoA and reduced deposition in adipose tissue. The influence of AMPK on lipogenesis and lipolysis is, hence, found via altered concentrations of malonyl – CoA. When the concentration of malonyl – CoA is low in the hypothalamus, the expression of orexigenic pathways with their corresponding neuropeptides NPY

and AgRP is stimulated, whereas the anorexigenic peptides POMC, α – MSH and CART are depressed, resulting in increased feed intake and decreased energy expenditure. Conversely, when the concentration of malonyl – CoA is high, the expression of orexigenic peptides is reduced and the expression of anorexigenic peptides is increased, whereby feed intake decreases and energy expenditure increases [2].

The second major energy sensing system, mTOR, also responds to changes in energy status of cells, but, in contrast to AMPK, it is activated by high amounts of available nutrients and energy, and thus a high ATP: AMP ratio. In addition, mTOR is activated by amino acids, mainly leucine. The mTOR sensing of energy status is through AMPK, which inhibits some essential mTOR dependent metabolic pathways. Therefore the activation of mTOR and AMPK is inversely related. A major role of mTOR is controlling cell growth, including protein synthetic processes. mTOR is active in peripheral tissue such as liver and skeletal muscle, but also in the hypothalamus, particularly in the PVN and ARC nuclei. In the ARC, it is co-localized with the melanocortin system neuropeptides, approx. 90% with the NPY/AgRP neurons and 45% with the POMC/CART neurons. The mTOR activity is low when the energy status of an animal is low, whereas its activity is high in well-fed, satiated animals. The feed intake controlling effect of mTOR has been demonstrated by intracerebroventricular administration of its inhibitor, rapamycin, which lead to a significantly increased feed intake. There is evidence that the feed intake reducing effect of leucine, which is related to reduced expression of the orexigenic NPY mRNA, is exerted via the mTOR pathway: when rapamycin was co-administered with leucine, no depressing effect of leucine on feed intake was recorded. Furthermore, rapamycin did not reverse the negative effect on feed intake and body weight of administration of an agonist for POMC and α – MSH melanocortin receptors, suggesting that the action of mTOR is to depress the activity of orexigenic peptides, but not to stimulate the anorexigenic peptides in the hypothalamus [2].

To conclude, the quantitative importance of the two major energy sensing systems, AMPK and mTOR, to feed intake regulation in growing pigs is presently unknown, but in restrictedly fed pigs the AMPK system would be the most activated, and it would drive the regulation of lipogenesis and lipolysis in the direction of lipolysis, and it would also strive to save energy by decreasing energy expenditure. Conversely, in ad libitum fed pigs the mTOR system can be expected to dominate: mTOR senses nutrient and energy status, particularly amino acids, and especially leucine. High nutrient availability activates mTOR and results in suppression of orexigenic pathways and increased energy expenditure. High dietary supply of leucine will have a depressing effect on feed intake.

6. Integration of metabolic control of intake

As described in paragraphs 4 and 5, information from nutrients and metabolites in circulation and in the GIT, combined with hormonal and neural signals, transmitted via the vagus nerve to the brainstem and to centres in the hypothalamus, and information on energy status of the animal via AMPK and mTOR are combined and contribute to altering the expression of orexigenic and anorexigenic peptides in the hypothalamus, peptides that are involved in the long-term regulation of feed intake, energy expenditure and body composition. A few examples, based on Black et al. [2], are given below in order to illustrate how these metabolic signals are integrated in different situations.

If nutrient and energy supply is below the requirement for metabolic processes, or if an animal is feed deprived, this will be sensed in the hypothalamus as a high AMP:ATP ratio. In order to conserve energy and provide ATP for essential metabolic processes, AMPK activation is stimulated, resulting in declining concentration of malonyl – CoA, which in turn will stimulate the expression of the orexigenic peptides NPY and AgRP. Concomitantly, the expression of the anorexigenic peptides α – MSH and CART will be reduced. Because of the high activity of AMPK, mTOR activity will decline, with further positive effect on NPY expression. As fewer nutrients are available for metabolism, ghrelin secretion will increase, the animal will feel a sensation of hunger, and ghrelin will further stimulate the activation of AMPK. The low energy supply/feed deprivation will reduce body

fat content with declining concentrations of plasma leptin and insulin as a result. Low leptin and insulin will also contribute to increasing the expression of the orexigenic peptides NPY and AgRP. These combined factors will induce an increased feed intake and lowered energy expenditure (see Figure 19.1). This situation could, for instance, apply to a lactating sow with a very large litter that is not able to sustain its energy requirement with feed intake, only but has to mobilise body reserves.

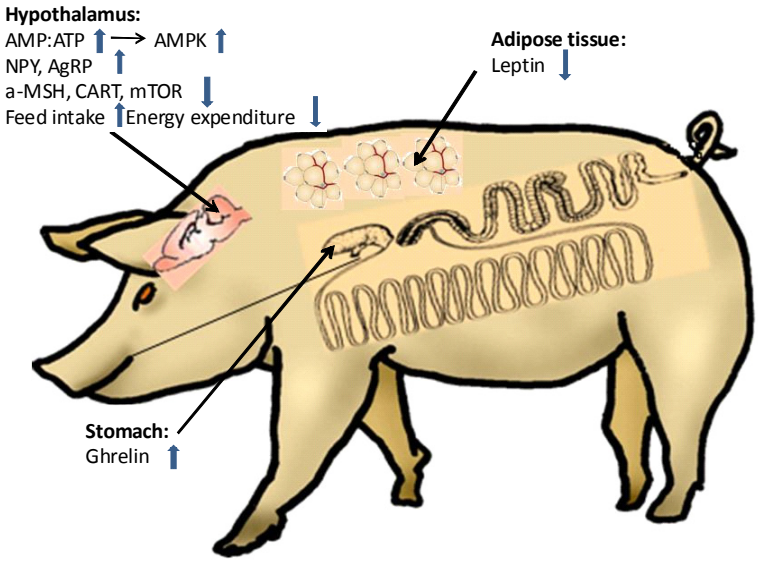

Figure 19.1. This figure exemplifies a pig given an energy supply below its need or being feed deprived. For explanatory text, see paragraph 6.

The next example concerns a well-fed animal, with ample supply of nutrients and energy. The animal has excess circulating concentrations of glucose, lipids or amino acids, and is in a state where nutrients, especially lipids, can reach the distal GIT in amounts sufficient to exert ileal brake function. Plasma concentrations of insulin and IGF-1, thyroid hormones and leptin will be high, whereas those of GH will be low. This animal has, moreover, considerable body fat reserves. It will therefore respond so that feed intake is reduced and energy expenditure increases. The presence of nutrients in the GIT will cause release of peptides from the intestine (CCK, GLP-1, OXM) and pancreas (pancreatic polypeptide), which are believed to exert long-term negative effects on feed intake acting via the vagus nerve through the brainstem and to the hypothalamus. Other peptides probably act directly on the hypothalamus: PYY from the intestine and insulin from the pancreas.

The adiposity status of the animal suggests that it has high circulating concentrations of leptin, and leptin will exert anorexigenic effects by depressing the expression of NPY and AgRP and stimulating the expression of POMC and CART. Moreover, high concentrations of leptin will augment the anorexigenic effects of some gut peptides (CCK, GLP-1, OXM). Some peptides exert their anorexigenic effects by decreasing the expression of NPY (PYY, CCK, pancreatic polypeptide) or stimulating the expression of the anorexigenic POMC (PYY, GLP-1, pancreatic polypeptide) (see Figure 19.2). This situation could be applicable to an ad libitum fed pig that consumes at will.

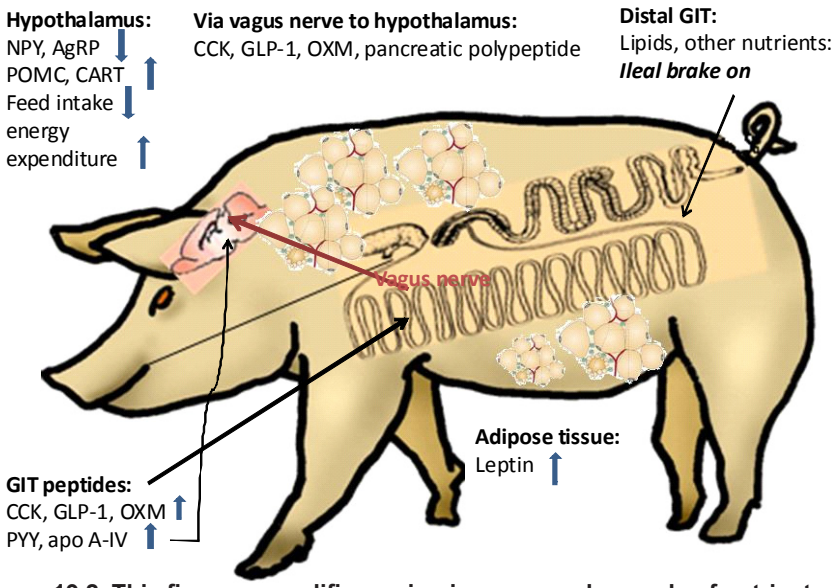

Figure 19.2. This figure exemplifies a pig given an ample supply of nutrients and energy. It consumes energy above its requirement. For explanatory text, see paragraph 6.

The animal described above was in positive energy balance and had a surplus of energy available for metabolic processes. In terms of AMP:ATP ratio, this will be reflected in a low ratio, and therefore the activation of AMPK is low, and the concentration of malonyl – CoA in the hypothalamus will be high. The high concentration of malonyl – CoA will result in decreased expression of the orexigenic peptides NPY and AgRP, whereas the expression of the anorexigenic peptides POMC and CART will be enhanced.

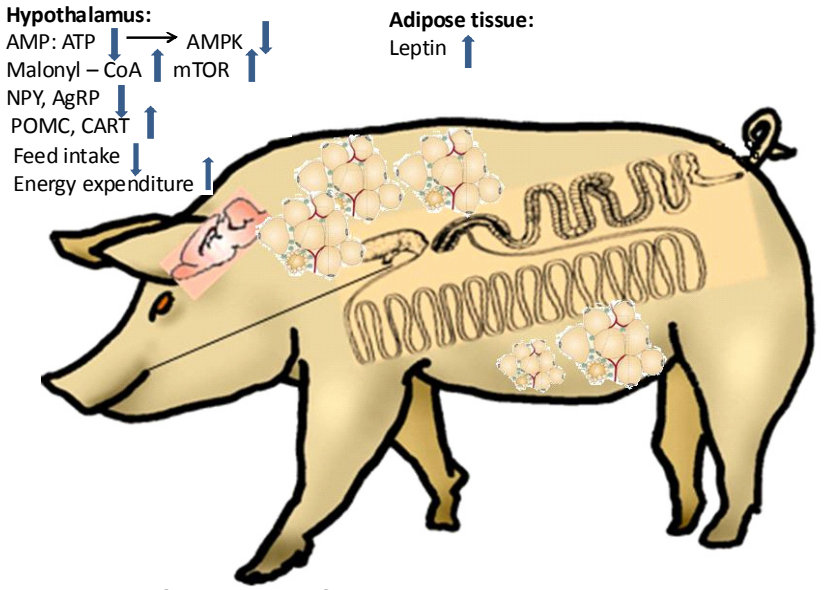

Figure 19.3.This figure exemplifies how the energy sensing systems AMPK and mTOR respond to a feeding situatuion similar to that in Figure 19.2. For explanatory text, see paragraph 6.

These effects will be further augmented because mTOR will be activated by the low activation of AMPK and by high circulating concentrations of leptin and insulin, which are caused by the high adiposity of the animal. This stimulated expression of anorexigenic peptides and decreased expression of anorexigenic peptides will cause the animal to feel satiated, and feed intake will decrease and energy expenditure increase in order to return to a stable energy balance (see Figure 19.3).

7. Diet selection

7.1. Dietary protein content

Animals given the choice between an imbalanced and a balanced feed may, in some situations, be able to select the balanced one, or to correct a deficiency by increasing their intake of a diet supplemented with the deficient nutrient. Moreover, animals have been shown to have the ability to select a diet corresponding to their nutritional requirements when given the choice between two or more imbalanced feed sources. The concept of diet selection is sometimes used in practical feeding, and many examples of successful results are found in research with poultry and pigs. Diet selection experiments and the practice of choice feeding usually focus on animals' ability to select a diet with appropriate protein content from two feeds, either high or low in protein, and yet being able to perform normally on the selected diet. Below, some examples of successful diet selection experiments are described to visualise the principle. However, Danish experiences of diet selection for growing pigs have been less successful, and the system is not used in practise in Denmark. In the studies described below the pigs had been trained to the feeding situation, and moreover, they represent genotypes other than those used in Denmark, and in one case pig breeds with very different genotypes were used.

Growing pigs show an ability to select feed to provide them with a protein supply that is appropriate to support their potential growth and protein retention. This has, for instance, been demonstrated in pigs from weaning to 30 kg given diets with crude protein (CP) contents of 125 (L), 174 (A), 213 (B) and 274 (H) g/kg, respectively. When pigs were given the choice between pairs of non-limiting feeds (LB, LH, AB and AH), pigs on all diet combinations selected a similar amount of protein (range: 202-208 g CP/day), and performed similarly. The selected amount of protein declined as pigs grew older. These results suggest that pigs are able to choose a balanced diet when given a choice between suitable diets, and that they are able to change dietary composition according to their requirements. In a following experiment, pigs were fed on single diets with high (278 g CP/kg) or low (134 g CP/kg) protein content from weaning until 16 kg LW in order to create two groups of pigs with different body composition. This goal was achieved, and from 16 until 33 kg LW, the pigs previously given L or H were given either L or H alone or a choice between L and H. When given the choice between L and H, those previously given L alone chose a diet with significantly more protein than those given H in the first period (233 vs 175 g CP/kg). The pigs from L had a higher daily gain, a higher daily feed intake and were more efficient than those that had started on diet H. In addition to the ability to select feed to their needs, the animals, when given the choice, were able to correct effects of a previous mis-feeding.

The studies reported above were performed with young pigs in a period of very rapid growth. It has been suggested that older growing animals do not have a similar ability to choose a diet according to their protein requirement, but in a study with boars from 43 to 103 kg LW it was shown that boars given the choice between 119 g CP/kg and 222 g CP/kg systematically changed the proportion eaten of each diet so that their protein intake declined from 193 g CP/kg during the first 7 days of the study to 146 g CP/kg during the last 7 days of the experiment. The choice-fed pigs performed equally well and were equally efficient as pigs fed on the high protein diet only. It was concluded that it would be possible to give pigs the choice between two suitable feeds throughout the growing – finishing period instead of changing the dietary composition of a single feed.

Another elegant example of how pigs with different requirements are able to select diets according to their needs was given when the performance of a European breed selected for high growth performance and lean deposition was compared with Chinese Meishan pigs with a low weight gain and a high potential for fat accretion when given either a single feed with high protein (HP) content or the choice between an HP and a low protein (LP) feed. The European breed selected more than 50% of its intake from the HP feed resulting in the selected feed having a protein content slightly below that of the single feed, but providing the same growth rate and deposition of protein and fat as the animals fed the single feed. The Meishan pigs, on the other hand, selected only slightly more than 10% of their feed from the HP diet, and the protein content of the selected diet was 50

g/kg lower than that selected by the European breed. The feed intake of the diet selecting Meishan pigs was higher than that of animals fed the single HP diet, and they had a higher growth rate and protein and fat deposition. This demonstrates very clearly that growing pigs are able to select feed to provide their requirement to realise their potential growth rate according to the inherent growth plan.

7.2. Appetite for specific nutrients: amino acids

Specific nutrients may influence the appetite of the animal, and generally, profound nutrient imbalances have an appetite-depressing effect. Therefore, both a severe deficiency and an excess of a certain nutrient is likely to reduce the intake. By giving animals a choice between balanced and imbalanced diets, attempts have been made to evaluate whether an animal has an appetite for a specific nutrient, and in that case, if this can be applied successfully if the animal is given the opportunity to select its diet from a choice of two or several feeds.

Appetite for specific nutrients has, at least to some extent, been demonstrated in most domestic animals. In order to achieve conclusive results in such experiments, certain conditions should be fulfilled. The animal ought to be at least marginally deficient in the nutrient of which a specific appetite is to be demonstrated. Furthermore, the animals have to be able to discriminate between the different feed choices they are offered. This can be done either by the colour, the flavour, the taste or the position in which the feed is placed. To facilitate the discrimination process for the animals, each experiment ought to be preceded by a training period, during which the animals learn to recognise the various feeds offered. Hence, as demonstrated above, pigs are efficient in selecting a protein intake to support their requirements. There is also evidence for specific appetites for some amino acids, but the animals are seldom able to balance their diets to match their demands exactly. When appetite for specific amino acids has been investigated in growing pigs, balanced diets have been preferred to imbalanced, and it has been suggested that imbalanced diets cause malaise, and that the pigs therefore learn to avoid such diets. Diets with 4% excess of lysine, threonine and arginine were preferred to those with excess of methionine and tryptophan. When pigs have been given the choice to select for lysine it has, in many cases, not been possible to show a consistent selection of the amino acid especially among growers, whereas more recent experiments with weaners suggest that the animals preferred the diets with higher lysine content (reviewed by [13]. The feed intake depressing effect of excess leucine, caused by stimulation of mTOR activation was described under 5.5.

8. Anti-nutritional factors

Several feed ingredients used in pig nutrition may contain anti-nutritional factors. The content of some of them may be reduced as an effect of feed processing, e.g. thermal treatment. The presence of anti-nutritional factors may affect feed intake negatively, but results from experiments into such effects are not always clear-cut, probably because other factors related to the feedstuffs used may cause confounding effects. Another problem hampering this type of experimental work is that it is seldom possible to feed the anti-nutrient in pure isolated form. The impact of anti-nutritional factors on pigs' voluntary feed intake was recently reviewed by Clasadonte and van der Poel [4] and this section is to a major extent based on their review.

Anti-nutritional factors make up a very diverse group of compounds, some being proteins (enzyme inhibitors, lectins) and others relatively low weight constituents (tannins, oligosaccharides, saponins). Owing to their very diverse physico-chemical properties their physiological action will also be highly diversified. Therefore, anti-nutritional factors are classified in relation to their action, i.e. into

- factors depressing digestion of or metabolic utilization of proteins (protease inhibitors, lectins, saponins, and polyphenolic compounds)
- factors depressing the digestion of carbohydrates (amylase inhibitors, polyphenolic compounds, flatulence factors
- factors inactivating vitamins or increasing the requirement of certain vitamins (antivitamins)
- factors that stimulate the immune system (antigenic proteins)

Examples of feedstuffs with content of protease inhibitors are soybeans and peas which contain trypsin inhibitors. Lectins are carbohydrate-binding proteins and are found e.g. in beans. Tannins are water-soluble polyphenolic compounds that can be found in e.g. sorghum, barley, rapeseed or legume seeds such as common beans and faba beans. Glucosinolates are mainly found in full fat seeds and seed meals of the genus Brassica, e.g. rape seeds and rape seed meal.

Main conclusions of the review by Clasadonte & van der Poel [4] were that they could not find any clear and consistent linear relationship between the level of anti-nutritional factors and feed intake in pigs. This was ascribed to presence of other undesired factors in the diets, or feed processing effects. They did, however, identify two different groups of ingredients, namely one with such that do not have any consistent effect on feed intake in pigs (peas, rapeseed and lupins) and a second group that when fed in the raw state systematically impairs feed intake (soybeans and Phaseolus beans). Both soybeans and Phaseolus beans are, however, normally only consumed after removal of heat-labile anti-nutritional factors. The authors also made a second grouping of anti-nutritional factors into such that have a direct impact on gut function (e.g. trypsin inhibitors, lectins and polysaccharides) and others that reduce the palatability of the feed so that pigs decrease their feed intake (e.g. tannins, alkaloids, glucosinolates, saponins). Finally, it was concluded that when studying effects of anti-nutritional factors on animal performance, it is not sufficiently informative to examine only feed intake.

9. Feed processing

The impact of feed processing on voluntary feed intake is most pronounced for newly weaned pigs, and processing strategies aim to stimulate feed intake both by the choice of dietary ingredients (e.g. high protein quality, high energy concentration, good palatability) and feed processing technology (e.g. particle size, heat treatment for gelatinization of starch, pelleting). However, a detailed description of how different feed formulation and processing strategies affect the feed intake of weaned pigs is beyond the scope of this chapter.

10. Environment

The thermal environment in which an animal is kept will influence the feed intake to a considerable extent. Animals kept in cold environment need energy for cold thermogenesis, and their intake will increase correspondingly. In the zone of thermal comfort the animal has no need to use energy for thermoregulation, and hence its heat production is at a minimum, given its rate of growth. For animals kept in a hot environment the capacity to lose heat is a factor that may influence feed intake. Pigs growing at a fast rate and metabolizing large amounts of feed will consequently increase their heat production and the need to dissipate excess heat will increase. If animals are kept in a thermal environment above their thermal comfort zone the feed intake will decline at a rate that has been estimated to 1 g per 1 °C above maximum comfort temperature per kg pig live weight, which can be expressed by the following equation:

$$\text{Feed intake reduction (g/day)} = W(T - T_c)$$

where W is the live weight in kg, T is the effective ambient temperature and T_c is the temperature at which the pig experiences optimum comfort. An example based on an 80 kg pig indicated a daily feed intake of 3.2-3.3 kg when temperature ranged from 10 to 20 °C. When ambient temperature dropped to close to 0 °C, intake increased to about 3.8 kg whereas an increase in ambient temperature to 30 °C resulted in a reduction in intake to slightly below 2.0 kg. The rate of air movement also influences the ability to dissipate heat and avoid thermal stress, and it can be assumed that an increase in air movement of approx. 10 cm/s is equivalent to a decrease in temperature of 1 °C [8].

The profound influence of ambient temperature on feed intake, heat production and energy retention in growing pigs has been demonstrated in studies where pigs with initial body weights in the interval 21-38 kg were kept at 10, 15, 20, 25 and 30 °C and pigs at each temperature were fed either at maintenance (M), 2M, 3M or ad libitum. The main results are presented in Table 19.2.

Table 19.2. Effect of environmental temperature and level of energy supply on feed intake, intake of metabolisable energy (ME), heat production (HE) and the retention of protein and fat (after [14] and [15]).

Environmental temp., °C	Feed intake, g/ $kg^{0.75}$ d	ME intake, kJ/$kg^{0.75}$ d	HE, kJ/$kg^{0.75}$ d	Protein retention, g/ $kg^{0.75}$ d	Fat retention, g/ $kg^{0.75}$ d
Maintenance energy supply					
10	49	571	593	0.6	-0.9
15	43	504	604	1.2	-3.2
20	42	495	469	0.9	0.1
25	38	455	425	1.3	0
30	38	455	484	1.8	-1.8
Ad libitum energy supply					
10	169	1965	1009	10.4	17.8
15	135	1591	854	7.5	14.1
20	140	1655	863	8.2	15.0
25	121	1406	714	6.5	13.5
30	103	1202	765	5.2	7.8

ME intake of ad libitum fed pigs decreased profoundly from 10 °C to 30 °C, and heat production was minimal between 20 °C and 25 °C, but increased when animals were kept at 30 °C, suggesting that this temperature was above the upper critical temperature for animals at all feeding levels. The critical temperature depended on feeding level and decreased from 23.1 °C at M to 16.7 at ad libitum, corresponding to approximately 4M. This demonstrates clearly that well-fed animals withstand far lower ambient temperatures than animals that are restrictedly fed. Energy retention, at all feeding levels, peaked between 20 °C and 25 °C, but most animals fed M were in negative energy balance.

11. Feed intake during infection

Health status is an important factor with influence on VFI, and in pigs, as in other species, infection causes anorexia, the extent of which may vary from a reduction in feed intake of only 10-20% to complete feed refusal. Reduced feed intake in conjunction with infection is an important causative factor for impaired animal performance, including poor feed utilization, growth and reproduction. There appears to be a considerable variation in when and to what extent anorexia occurs, and that such variation depends on which kind of pathogen is causing the infection. Further, systematic investigations into factors causing variation are almost lacking. In addition, when studies on duration of anorexia have been performed, the feed intake has most often been averaged over periods that have included different phases of anorexia development, duration and recovery. The general pattern of anorexia development is often similar among pathogens, but it develops according to different time scales, where infections with bacteria and viruses often develop considerably more rapidly than those caused by larger pathogens. When the infection occurs there is a *lag phase* before anorexia is noticeable. This lag phase may be as short as less than one day in the case of

bacterial infection whereas its duration can be several weeks after infestation with gastro-intestinal parasites. Feed intake then declines over a period that also may be highly variable in length, from a few hours to several weeks to reach its lowest level, the *extent of anorexia*. This lowest level of intake will remain for a certain time period. This phenomenon called the *duration of anorexia* can vary in length from some days to several weeks, the consequences on host performance being related to length of the period. When the host animal has overcome the effects of the infection, a recovery period will commence. The *rate of recovery* will also vary and result in feed intake returning to, or even exceeding, the level before infection.

Response to an infection can be affected both by nutritional and other environmental factors. How the lag phase and the level of reduction in feed intake are affected by bacterial and viral infections is little investigated, and most data regarding parasite infections derives from ruminant animals. The influence of protein and amino acid supply to pigs on the extent of anorexia has been investigated in pigs kept in a clean environment or in an environment causing high immune system activation. In this study, the feed intake of uninfected and challenged animals was similar at the lowest level of lysine (6 g/kg diet) whereas challenged animals only consumed 85% of the intake in the uninfected animals when the double amount of dietary lysine was fed. The level of feed intake of challenged animals was then the same as at the low lysine level. The level of gain was suppressed at all levels of lysine supply, but suppression increased with increasing level of dietary lysine. Although other studies have failed to document any effect of protein/amino acid supply on feed intake during infection, these results would suggest that when animals are fed on a protein/amino acid level that is below the level supporting their maximum performance, feed intake of uninfected animals may be constrained for other reasons, and a bacterial challenge incurs no further constraint. The challenged animals, however, expressed both anorexia and impaired performance when lysine was supplied at levels supporting a good animal performance. The effect of dietary energy density on the extent of anorexia has only been investigated in few experiments in pigs, and results indicate that there is no relation between energy density and the extent of anorexia. Dietary effects on the duration of anorexia have mainly been investigated in ruminants, and results suggest that high quality diets shorten the duration of anorexia. Similarly, solid experimental evidence of dietary effects on rate of recovery is lacking, but again it is fair to assume that high-quality diets support a rapid recovery.

Although direct data is lacking on how feed intake in pigs of different genotype is influenced by a pathogen challenge, response in other performance and immune traits suggests that genotype has a significant impact on anorexia, both regarding the level of feed intake depression and the duration of the anorexia (entire section based on [9]).

12. Models to predict feed intake

Along with the increased capacity for lean tissue growth and the simultaneous reduction in voluntary feed intake in pigs, the need for predicting feed intake has become increasingly more pronounced. Whereas unimproved pig breeds had to be fed restrictedly in order to avoid excessive fat accretion, the voluntary feed intake of modern pig breeds may be a constraint to achieving optimal growth and protein accretion in the body. Over the last many years, different model approaches have been used and models of different complexity have been developed. The more complex a model is, the more likely it is to make good predictions, but, on the other hand, it can be difficult to collect all information to feed into the model. Pigs of different genetic origin can be expected to have different voluntary feed intake, and therefore genetic background ought to be included in the model, but so is seldom the case. Some models apply to a certain weight or age interval, and may give erroneous results if applied to other weight/age ranges. Very few models of animal systems have been truly mechanistic, because of the enormous complexity of this type of systems. Models used for prediction of feed intake most often have been developed at a “conceptual level”, where concepts believed to control a process can be described mathematically. The most commonly used concepts for predicting voluntary feed intake in pigs have been exemplified in a review by Black [1],

and below these concepts are presented briefly, with short comments on their ability to make correct estimates:

Simple statistical fit of algorithms to experimental results

For instance, NRC [11] presents two simple models, a second order equation based on live weight for pigs from 5 to 15 kg live weight and a cubic function, similarly based on live weight for heavier pigs. For obvious reasons, the second order equation will give incorrect estimates for body weights above those corresponding to summit feed intake; indeed it predicts a negative intake for animals of 40 kg and above. Another constraint may be that data for pigs that are heavier than normal slaughter weight is limited, and therefore predictions outside the weight range for which data is abundant become less accurate. This is demonstrated by prediction equations based on simple algorithms having shown to over-estimate VFI of pigs heavier than 70-80 kg.

Intake is predicted from the sum of the energy needs of the animal for maintenance and for protein and fat deposition. The energy needs are then related to the energy density of the diet and voluntary feed intake is predicted.

In this approach, constraints caused by e.g. different climatic conditions, housing system, stocking density are not included in the model.

As above, but constrained with different dietary, environmental and social factors

In this type of model, it is assumed that an animal will eat sufficiently to satisfy its genetically determined requirement for energy and nutrients, but that environmental factors as mentioned above will either increase or decrease the intake from the potential. Presently, this type of model is probably the most commonly used and it may provide accurate predictions.

Maximization of the efficiency of oxygen utilization

This concept proposes that there are both costs and benefits from consuming feed. The benefits are the net energy consumed for maintenance and productive processes, and the costs are associated with oxygen consumption by tissues that cause accumulated damage to tissues, e.g. ageing and oxidative damage to cell structures. It was speculated that an animal ceases eating when it has reached an optimum efficiency in the utilization of energy, i.e. when the net energy intake per liter oxygen was maximized. However, when comparing this concept with the “potential-constraints” type model it was shown that the “oxygen-efficiency” type model made poorer predictions than the “potential-constraints” type model, especially for high bulk type diets fed in cold environments.

The minimal total discomfort theory

This theory proposes that the animal learns from experience what causes physical or metabolic discomfort, and integrates these signals so that the discomfort it experiences is minimized. It comprises calculation of the mismatch between the current value of a resource and its optimum, and such calculations are made for every resource that is considered. For every resource, the square of this difference is determined, and the sum of the squares for all resources is calculated. The minimal total discomfort is then calculated as the square root of the summed value, and the feed intake corresponding to this minimal total discomfort value will be selected. The minimal total discomfort model has been demonstrated to predict results achieved with animals consuming low bulk and high bulk diets. However, the model will need further development and refinement before it can be used for practical purposes (section based on [1]).

13. Concluding remarks

Regulation of feed intake is, as is apparent above, a very complex process involving physical and metabolic processes. Physical constraints on intake are more important to intake regulation in

piglets and young growers, whereas metabolic factors have more impact on feed intake regulation in older growers and adult pigs. When contemplating feed intake regulation it should be born in mind that several complementary and redundant regulatory systems exist. This means that several pathways may be simultaneously involved in the regulatory processes, and that it can be difficult to discern which are the most important in a given physiological stage and feeding situation. This review has attempted to describe important regulatory processes, including brain centres that are important in feed intake regulation, important hormones gut- and neuro-peptides as well as systems sensing the energy status of the animals. Furthermore, feed characteristic such as taste, smell, nutrient composition, and the presence of anti-nutritional factors as well as environmental factors and health status influence feed intake. Information from all systems involved in feed intake regulation is sensed by the higher regulatory centres and integrated into a response that is the VFI. For an optimal performance of growing pigs, factors that put a constraint on VFI ought to be avoided, whereas knowledge on factors that may contribute to reduce feed intake can be useful in situations when restricted feeding is practised.

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