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Peptides and Feeding Behaviours of Animals

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Abstract. Peptides have been identified as one of the major factors modulating animal feeding behaviors. These peptides are divided into orexigenic and anorexigenic peptides. The orexigenic and anorexigenic peptides are involved in instigating and suppressing appetites thereby influencing feeding behaviours of the animal, respectively. At the centre of control of energy homeostasis or balance is the central nervous system (CNS), involving especially the lateral and ventromedial hypothalamus areas of the CNS. These regions of the CNS are accessible by peptides thus recognize peptides' signals via their receptors in these areas and act in the network to integrate the multiple inputs and thus aid in regulating appetite resulting in the 'set-point' of the animal. Therefore, the better understanding of the network activities of peptides modulating feed intake presents a huge therapeutic targets in enhancing healthy weights of the animal. Although there are many orexigenic and anorexigenic peptides, five peptides from each group, respectively were covered in this paper.

Key Words: Peptides, Orexigenic, Anorexigenic, Appetites and Animals

Introduction

There are many factors modulating feed intakes in animals, including humans. One of such factors are peptides. The mechanisms affecting feed intakes in animals are based on the 'dual-control theory of feeding' involving peptides (Lowell & Spiegelman, 2000). The dual-control theory is based on a homeostatic view of hunger and satiety. The main animal organ at the centre of the dual-control theory is the brain. There are two major areas of the hypothalamus involved in the theory. These are the lateral hypothalamus (LH) and the ventromedial hypothalamus (VMH). The LH is responsible in inducing feeding whereas the VMH is the 'satiety centre' and therefore responsible in signaling the animal to stop eating. Therefore, our better understanding of the mechanisms modulating feed intake based on the dual theory can open more opportunities in the provision of new pharmacological approaches in dealing with obesity and appetite disorders.

From the afore-stated, a decline in glucose activates the LH and activity within the LH gives rise to hunger. Hunger motivates the search for and consumption of food. The consumed food is broken down to release glucose or energy. The released glucose activates the VMH. Activation of the VMH causes a feeling of satiety. Satiety in turn inhibits further feed intake. Therefore, the balance between the activities of peptides in the LH and VMH brings the animal to a set-point mechanism desired by the farmer for value capture (Lowell & Spiegelman, 2000).

To this point, there are two major kinds of peptides. The appetite-stimulating peptides known as the orexigenic peptides and the appetite-suppressing peptides also known as the anorexigenic peptides. These two categories of peptides normally receive signals from the LH and VMH to influence feeding by either inducing or inhibiting feeding, respectively (Finer, 2002). Subsequently, activities of the orexigenic peptides if not checked makes the animal to suffer from hyperphagia which sets in obesity whereas anorexigenic peptides aid the animal to control body weight through a set-point mechanism (Badman & Flier, 2005). There are many orexigenic and anorexigenic peptides. However, in respect to this paper, five peptides from each group will be briefly covered in terms of their sites of productions and mechanisms via which they influence the feeding behavior of the animal. The five peptides for each group are shown in Table 1.

Table 1. Orexigenic and anorexigenic peptides regulating feed intake

S/No.	Orexigenic Peptides	Anorexigenic Peptides
1	Neuropeptide Y (NPY)	Leptin
2	Agouti-Related Protein (AGRP)	Alpha-melanocyte-stimulating hormone (α-MSH)
3	Ghrelin	Cholecystokinin (CCK)
4	Galanin (GAL)	Peptide YY (PYY)
5	Melanin-concentrating hormone (MCH)	Cocaine and amphetamine regulated transcript (CART)

Orexigenic Peptides

Neuropeptide Y (NPY)

NPY is a thirty-six- (36)-amino acid peptide and is produced from the arcuate nucleus (ARC) neurons of the lateral hypothalamus. When produced its most noticeable effect is the stimulation of feeding via its actions in the LH producing hunger signals thereby inducing the animal to eat. NPY is thought to be the most potent appetite-stimulating peptide probably due to the fact that most anorexigenic peptides target NPY in exerting their anorectic effects. Five NPY receptors have been identified, namely Y_1, Y_2, Y_4, Y_5 and Y_6 to be involved in the feeding attributes of NPY. Amongst these receptors, the Y_5 receptors have been identified as the main receptors of the NPY peptide that mediate the potent feeding effects of NPY (Marsh *et al*., 1998). This is more so as the Y5 receptor is expressed at relatively high levels in the LH, close to the site where NPY acts most potently to stimulate feeding (Williams *et al.*, 2000). It is because of this function of NPY in feeding behavior of the animal that is solely responsible for NPY mRNA levels and NPY release in the ARC in respect to responses to changes in energy status, being increased after fasting and food restriction and decreased after re-feeding (Swart *et al*., 2002).

Agouti-Related Protein (AGRP)

AGRP is a 132-amino acid peptide. AGRP works in synergistically with NPY as they are usually co-produced. Within the central nervous system (CNS), like NPY, AGRP is expressed exclusively in the ARC and AGRP mRNA co-localizes with NPY mRNA in 95% of NPY positive cells in the ARC (Broberger *et al*., 1998). Uniquely, AGRP acts as an endogenous antagonist of the melacortin-3 (MC3R) and melacortin-4 (MC4R)-receptors in stimulating feeding (Ollmann *et al.*, 1997) since they are the receptors mainly involved in the action of α-MSH in suppressing feed intake. Furthermore, AGRP is more important during conditions of high energy requirements, such as pregnancy and lactation under which it has been shown to be more highly expressed (Sorensen *et al.*, 2001) and serves as one of the ways AGRP modulatory role in feeding is achieved.

Ghrelin

Ghrelin is a peptide composed of 28-amino acids. Ghrelin is a gut peptide as it is secreted in the duodenum, jejunum, ileum and colon. In the intestine, ghrelin concentration gradually decreases from the duodenum to the colon (Sakata *et al*., 2002). Ghrelin plays important role in energy homeostasis. Ghrelin induces positive energy balance by decreasing fat utilization without markedly changing energy expenditure or locomotive activity (Sakata *et al*., 2002). Plasma levels of ghrelin are regulated by food intake, rising during fasting and immediately before meals and falling after food intake (Cummings & Shannon, 2003). Overall, ghrelin expression is directly modulated by energy intake and nutritional signals, such as blood glucose and ingestion of fat or carbohydrate (Sakata *et al*., 2002).

Galanin (GAL)

GAL is a 30-amino acid peptide. GAL co-exists with NPY. However, GAL involvement in inducing feed intake has been shown to have preference for fat consumption (Lang & Kofler, 2011). It has also been reported that GAL increases fat consumption but reduces energy expenditure indicating that it accelerates the rates of hyperphagia and obesity (Lang & Kofler, 2011). To this point therefore, high plasma levels of GAL is an indication that the animal would prefer fat ingestion compared to other nutrients.

Melanin-Concentrating Hormone (MCH)

MCH is an orexigenic peptide consisting of 19-amino acids. It is highly expressed in the LH within the hypothalamus. MCH triggers feed intakes by arousing the NPY/AGRP signals for the need of the animal to eat. Therefore, one of the first lines of receiving hunger signal by the animal for feeding is via the activity of MCH in the LH via the NPY/AGRP axis (Saper *et al*., 2002).

Anorexigenic Peptides

Leptin

Leptin is the major anorectic peptide consisting of 167-amino acids that coopts its cohorts in the coordination of appetite suppression. It is the most potent known protein that suppresses appetite and regulate energy expenditure. Leptin is secreted or produced mainly by adipocytes, although it has been found in the stomach and the pituitary gland. Nevertheless, the adipose tissue (AT) remains the main source responsible for more than 95% of leptin production (Rolls, 2011). Leptin production correlates positively with AT mass. In humans, there is a highly organized pattern of leptin secretion over a 24-h period. In general, the circadian pattern is characterized by basal levels between 08:00 and 12:00 hours but rises progressively to peak between 24:00 and 04:00 hours and receding steadily to a nadir by 12:00 hours (Sinha *et al*., 1996). It should be noted that the nocturnal rise in leptin secretion is entrained to mealtime probably due to cumulative hyperinsulinemia of the entire day (Sinha & Caro, 1998). Leptin exerts its effects via the ARC where both NPY and AGRP neurons express leptin receptors. Leptin inhibits NPY and AGRP neurons activities and activates cocaine and amphetamine-regulated transcript (CART) neuron. CART is a potent anorectic peptide that blocks or inhibits the orexigenic activities of NPY and AGRP resulting in reduced feed intake (Wynne *et al*., 2005). Leptin also has been demonstrated to enhance the satiating effect of CCK in the gut (Harrold *et al*., 2012).

Alpha-Melanocyte-Stimulating Hormone (α-MSH)

This an anorectic peptide composed of 13-amino acids. It is one of the peptides leptin instigates its production in the VMH. It exerts it effects by antagonizing the activities of MCH at its most feed-inducing receptors or sites, namely, MCH 3 and MCH4**.** α-MSH inhibits feed intake by de-firing the activities of MCH at its potent receptors for increased feed intake, that is, at MCH3 and MCH4 leading to reduced feed intake (Pritchard *et al.*, 2002).

Cholecystokinin (CCK)

CCK is a 58-amino acids peptide. CCK is released post-prandially from the small intestine (Murphy & Bloom, 2006). Furthermore, CCK is normally released in response to saturated fat, long chain fatty acids, amino acids and small peptides that would normally result from digestion. CCK is involved in appetite reduction in its role on food intake. Nevertheless, CCK is mostly involved in the short-term control of food intake together with the distension of the upper gastrointestinal tract. Thus, it is the major peptide that senses when the small intestine

is empty and instigates the call for food withdraw from the stomach into the intestine (Konturck *et al.*, 2004; Badman & Flier, 2005) and simultaneously signals the NPY/AGRP axis to stop firing for feeding (Badman & Flier, 2005). In humans, intravenous administration of physiological doses of CCK reduces food intake and increases the perception of fullness (Lieverse *et al.*, 1995). CCK also exerts its control of feed intake by acting as an antagonist to the actions of NPY in inducing feed intake when released (Lieverse *et al.*, 1995) as earlier stated.

Peptide YY (PYY)

PYY is a 36-amino acids peptide. PYY is secreted in the gut in proportion to caloric intake and has it receptors in the LH. Plasma PYY levels rise within 30 minutes of a meal and in humans circulating levels plateau at 1-2 h post-prandially and remained elevated for up to 6 h (Batterham *et al.*, 2003). Protein-rich meals cause the greatest increase in PYY levels compared to other macro-nutrients. PYY when released serves as antagonist to NPY in the ARC, thereby deactivates the appetite-stimulating properties of NPY.

Cocaine and Amphetamine Regulated Transcript (CART)

CART is a 116-amino acids peptide. CART is another potent appetite-suppressing neuropeptide produced at the VMH but has its action in the LH. Thus, CART exerts its anorectic effect by antagonizing the actions of NPY and AGRP in the LH of the animal (Li *et al*., 2002).

Conclusions

Peptides are one of the major factors that modulate animal feeding behaviors. These peptides are divided into orexigenic and anorexigenic peptides. The earlier group instigates or induces feeding while the latter group suppresses feeding, respectively. The control of energy homeostasis or balance largely depends on the central nervous system (CNS), especially the LH and VMH areas of the CNS. These regions of the CNS concerned with the control of energy homeostasis are accessible by peptides that recognize peptides' signals via their receptors in these areas and act in the network to integrate the multiple inputs and thus aid in regulating appetite leading to the 'set-point' of the animal. Thus, the better understanding of the webbing of network activities modulating feed intake presents a huge therapeutic targets in enhancing healthy weights of the animal.

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