ABSTRACT: Nutrient ingestion triggers numerous changes in gastrointestinal (GI) peptide hormone secretion that affect appetite and eating. Evidence for these effects comes from research in laboratory animals, healthy humans, and, increasingly, obese patients after Roux-en-Y gastric bypass (RYGB) surgery, which has marked effects on GI hormone function and is currently the most effective therapy for morbid obesity. Increases in cholecystokinin (CCK), glucagon-like peptide-1 (GLP-1), and peptide tyrosine tyrosine (PYY) and decreases in ghrelin secretion after meals are triggered by changes in the nutrient content of the intestine. One apparent physiological function of each is to initiate a reflex-like feedback control of eating. Here we briefly review this function, with an emphasis on the controls of their secretion. Each is secreted from enteroendocrine cells that are directly or indirectly affected by caloric load, macronutrient composition, and other characteristics of ingested food such as fatty acid chain length. In addition, digestive hydrolysis is a critical mechanism that controls their secretion. Although there are relatively few data in agricultural animals, the generally consistent results across widely divergent mammals suggests that most of the processes described are also likely to be relevant to GI hormone functions and eating in agricultural animals.

Key words: cholecystokinin, ghrelin, gastrointestinal peptides, glucagon-like peptide-1, peptide tyrosine tyrosine
that most of the processes described here are also likely to be relevant to agricultural animals.

**GHRELIN**

Ghrelin is secreted mainly by X/A-like cells in the fundus of the stomach and, unique among GI hormones, stimulates eating. Its concentrations increase during fasting and decrease after meals, and intravenous infusion of ghrelin in both humans and animals significantly increases meal size, consistent with an acute role in meal initiation (Tsop et al., 2001; Ueno et al., 2005; Kirchner et al., 2012). In addition, basal ghrelin concentrations are decreased with overfeeding and increased by BW loss, indicating that ghrelin may be a tonic signal linked to body adiposity (Cummings et al., 2002; Williams et al., 2006). In 2008, Yang et al. (2008) showed that the enzyme ghrelin O-acetyltransferase (GOAT) catalyzes the conversion of ghrelin into its biologically active acylated form, indicating that GOAT is important in the pathogenesis of obesity. However, the physiological relevance of the effect of ghrelin on eating requires more research. For example, it is still unknown whether the physiological preprandial rise in circulating ghrelin is sufficient to trigger eating and whether ghrelin acts peripherally or centrally to control eating (Date et al., 2002; Arnold et al., 2006; Langhans and Geary, 2010; Kirchner et al., 2012).

Although the stomach is the major site of ghrelin secretion, it does not appear to contain the sensing mechanisms that suppress ghrelin secretion after meals, because nutrient exposure of the stomach alone is not sufficient to suppress ghrelin (Shiiya et al., 2002; Williams et al., 2003; Overduin et al., 2005). Rather, the available data indicate that the signals mediating the postprandial suppression of ghrelin originate further distally in the small intestine (Williams et al., 2003; Feinle-Bisset et al., 2005; Cukier et al., 2008; Ryan et al., 2012). In addition, changes in plasma insulin, intestinal osmolarity, or enteric neural signaling may mediate the suppression of ghrelin (Gelling et al., 2004; Cummings, 2006). A study by Shiiya et al. (2002) indicated that chemosensory mechanisms that respond to plasma glucose concentrations control ghrelin secretion.

Cummings and coworkers (Callahan et al., 2004) studied healthy volunteers receiving liquid meals with widely varied caloric content but equivalent volume and found that postprandial ghrelin suppression was proportional to the ingested caloric load. In addition, in studies in humans and rats they showed that carbohydrate and protein suppress ghrelin concentrations more effectively than lipid (Monteleone et al., 2003; Overduin et al., 2005; Cummings, 2006). In our own recent experiments, we found that intraduodenal lipid infusions are associated with a marked and progressive suppression of plasma ghrelin. Moreover, ghrelin suppression depends on lipid digestion into FFA and FFA with a chain length ≥C12 are more potent than FFA with a chain length <C12 (Feltrin et al., 2006; Degen et al., 2007).

Available data indicate that plasma ghrelin concentrations in cattle are similarly affected by fasting and energy repletion (Wertz-Lutz et al., 2006, 2010). For example, a study in dairy cows revealed a linear decline in pasture intake and postprandial ghrelin concentrations in cows fed nutrient-concentrate supplements (Roche et al., 2007). In addition, Wertz-Lutz et al. (2006) reported that intravenous infusion of ghrelin that produced fasting concentrations of plasma ghrelin were sufficient to increase time spent eating in cattle. Finally, a polymorphism in a gene controlling ghrelin deacetylation was reported to be associated with average energy intake and weight gain in cattle (Lindholm-Perry et al., 2012). The effects of fasting and refedding on ghrelin secretion and the eating-stimulatory effect of ghrelin administration have been replicated in pigs (Zhang et al., 2007; Dong et al., 2009). Fasting and refedding also affect ghrelin secretion in sheep, but tests of the effects of ghrelin administration on eating have produced both positive (Sugino et al., 2004; Grouselle et al., 2008) and negative (Iqbal et al., 2006; Krueger and Melendez, 2012) results, so that further work on this issue is warranted.

**CHOLECYSTOKININ**

Intestinal CCK is considered the paradigmatic GI control of eating because of the extensive evidence for its role in satiation in animals and humans (Gibbs et al., 1973; Kissileff et al., 1981; Geary, 2004). Cholecystokinin was purified as a 33 AA peptide by Mutt and Jorpes (1968). Although many different forms of CCK, including CCK-8, CCK-22, CCK-33, and CCK-58, were subsequently found in either the GI tract or in the brain, where it acts as a neurotransmitter (Rehfeld et al., 2007), recent data indicate that CCK-58 may be the only relevant endocrine form, with all smaller forms of CCK being proteolytic fragments (Eysselein et al., 1990; Liddle, 1997; Stengel et al., 2009). Intestinal CCK is released from duodenal I-cells. In addition to eating control, the putative physiological functions of CCK include the stimulation of the exocrine pancreas, liver, and gallbladder to secrete digestive enzymes and bile acids as well as the control of gut motility and gastric emptying (Liddle et al., 1986; Beglinger, 1994).

In 1973, Gibbs et al. (1973) first implicated CCK in the control of eating by showing that intraperitoneal injections of CCK into rats immediately before meals reduced meal size in a dose-dependent manner without signs of aversions and without reducing water intake in
thirsty rats. Since then, the ability of CCK signaling via the CCK-1 receptor to inhibit eating has been studied extensively in many species, with most of these studies using CCK-8, which is a full agonist for the CCK-1 receptor. Importantly, administration of CCK-1 receptor antagonists before meals selectively increases meal size in rats, mice, and humans. In addition, in both humans and rats, abnormalities of the CCK-1 receptor gene are associated with increased meal size, increased food intake, and overweightness in humans and rats (Miller et al., 1995; Moran et al., 1998; Marchal-Victorion et al., 2002; de Krom et al., 2007). However, CCK-1 receptor knockout mice are not hyperphagic or obese (Kopin et al., 1999). Whether this is related to the development of compensatory mechanisms is not clear. The satiating effect of exogenous CCK is very short-lived. The half-life of CCK is only about 2 to 3 min, and food intake is not affected when it is injected >15 min before a meal. Furthermore, the effect does not carry over from one meal to the next (Cummings and Overduin, 2007; Woods and D’Alessio, 2008). Whether or not this would limit the usefulness of CCK agonism for the long-term control of food intake is uncertain.

Available data indicate that CCK acts via an endocrine mode of action to inhibit eating in humans (Beglinger and Degen, 2004; Geary, 2004) but mainly via a paracrine mode in rats (Geary, 2004; Eisen et al., 2005). Evidence for the latter conclusion includes 1) there are only few reports of increased plasma CCK concentrations during meals in rats (Geary, 2004), 2) intravenous infusions of CCK-8 into the hepatic portal vein failed to reduce food intake (Greenberg et al., 1987), 3) under conditions in which intravenous infusions of a CCK-1 receptor antagonist failed to increase eating, local administration of the CCK-1 receptor antagonist into the superior pancreaticoduodenal artery increased food intake (Cox, 1998), and 4) intravenous infusion of a CCK antibody that decreased pancreatic amylase secretion failed to increase food intake whereas infusion of a small-molecule CCK-1 receptor antagonist under the same conditions had both effects, which strongly indicates a paracrine action because the antagonist but not the antibody would escape the circulation (Reidelberger et al., 1994). Cholecystokinin is thought to signal satiation via vagal fibers that directly innervate the tissue in close proximity to the site of CCK secretion. Vagal afferents have been shown to express CCK-1 receptors, and lesioning either the subdiaphragmatic vagal nerves or the dorsal vagal complex in the hindbrain has been shown to attenuate the anorectic effect of peripheral CCK (Smith et al., 1981; Edwards et al., 1986). Cholecystokinin may also limit food intake, in part, by slowing gastric emptying, as observed in both rodents (Moran and McHugh, 1982) and humans (Lal et al., 2004). Consistent with this hypothesis, Schwartz et al. (1993) showed that intravenous CCK infusion and small gastric loads synergistically increased vagal afferent firing in rats.

Liddle et al. (1985), who developed the first reliable assay for plasma CCK, found that glucose, lipid, protein, and AA all rapidly and potently stimulate CCK release. Subsequent studies have confirmed this and also demonstrated that protein and lipid are the most potent secretagogues (Himeno et al., 1983; Hopman et al., 1985; Pilchiewicz et al., 2007; Seimon et al., 2009). In our own experiments in humans, we recently showed that isoenergetic replacement of lipid by carbohydrate in intraduodenal infusions increased plasma CCK concentrations less than did lipid alone (Seimon et al., 2009). The exact mechanisms underlying CCK secretion are not fully understood. The majority of data indicate that digestion of proteins to oligopeptides and AA is required to efficiently release CCK (Gibbs and Smith, 1977; Cucer et al., 1990a; Darcel et al., 2005; Foltz et al., 2008). Similarly, when fat hydrolysis was blocked via lipase inhibition, CCK release was markedly suppressed (Hildebrand et al., 1998; Matzinger et al., 2000; Feinle et al., 2001, 2003). Moreover, fatty acids with chain length of ≥12 carbons stimulated CCK release much more than fatty acids with <12 carbon atoms (McLaughlin et al., 1998, 1999; Matzinger et al., 2000; Feltrin et al., 2004).

The control of eating by CCK in pigs has been studied extensively. As in humans, carbohydrates, proteins and lipids all stimulate CCK secretion in pigs (Houpt, 1984; Cucer et al., 1990b). The effects on eating of exogenous CCK, CCK-1 receptor agonism and antagonism, and intraduodenal fat infusion in pigs are all similar to their effects in humans (Anika et al., 1981; Gregory et al., 1989; Ebenezer et al., 1990; Parrott, 1993). In addition, active immunization against CCK increased food intake and body weight in pigs (Pekas and Trout, 1990). There has been less work on the satiating effect of CCK in ruminants. In cattle, fasting reduced and nutrient repletion increased plasma CCK concentrations (Suominen et al., 1998) and, under some conditions, changes in plasma CCK concentrations were associated with changes in food intake (Relling and Reynolds, 2007, 2008). In several studies in sheep, peripheral CCK administration did not reliably inhibit eating (Grovum, 1981; Baile and Della-Fera, 1984; Relling et al., 2011), perhaps because the ovine vagus appears to express predominately CCK-2 rather than CCK-1 receptors (Farningham et al., 1993). In both pigs (Parrott, 1994; Baldwin and Sukhchao, 1996) and sheep (Della-Fera et al., 1981; Della-Fera and Baile, 1984), there is evidence that CCK acts centrally to inhibit eating. In both species this appears to be a local effect of neural CCK released in the brain rather than an endocrine effect of intestinal CCK.
GLUCAGON-LIKE PEPTIDE-1

Glucagon-like peptide-1 is synthesized and secreted from endocrine L-cells, which are expressed most densely in the distal ileum and colon (Drucker, 2006; Holst, 2007). The bioactive form of GLP-1 is generated from GLP-1(1–37) and exists as 2 equipotent circulating molecular forms, GLP-1(7–37) and GLP-1(7–36NH2). Both forms are rapidly degraded by dipeptidyl peptidase-IV (DPPIV) to GLP-1(9–37) or GLP-1(9–36NH2). Dipeptidyl peptidase-IV is primarily located on the luminal surface of vascular endothelial cells and circulating in the plasma (Mentlein, 1999; Drucker, 2006; Holst, 2007). In addition to its incretin effect (Schmidt et al., 1985; Drucker, 2006; Holst, 2007), GLP-1 has been shown to inhibit eating in mice and rats (Turton et al., 1996; Meieran et al., 1999; Abbott et al., 2005; Chelikani et al., 2005). In humans, an early report by Flint et al. (1998) indicated that GLP-1 infusions enhanced fullness and reduced energy intake during an ad libitum test meal. Subsequent studies demonstrated that GLP-1 suppressed energy intake in obese and type II diabetic subjects (Gutzwiller et al., 1999; Naslund et al., 1999). However, some studies failed to demonstrate an anorectic effect of GLP-1 in humans (Naslund et al., 1998; Long et al., 1999; Brennan et al., 2005). Studies using specific GLP-1 antagonists are required to better establish a physiological role for GLP-1 in eating control in humans.

The anorectic effect of GLP-1 is thought to be mediated by GLP-1 receptors (GLP-1R; Bullock et al., 1996; Alvarez et al., 2005; Holst, 2007). The anorectic effect of exogenous GLP-1 is absent in transgenic GLP-1R deficient mice and can be abolished in intact mice with exendin(9–39), a selective GLP-1R antagonist (Baggio et al., 2004; Williams et al., 2009; Ruttimann et al., 2010). In addition, exendin(9–39) alone stimulated food intake in rats, at least under some conditions (Williams et al., 2009; Ruttimann et al., 2010; Asarian et al., 2012). Whether the crucial GLP-1R are in the brain, on vagal afferents, or elsewhere is unknown. As mentioned, DPPIV rapidly catabolizes GLP-1, and its plasma half-life is only 1 to 2 min. It is, therefore, unclear whether an endocrine mechanism of action via the systemic circulation is possible or whether intestinal GLP-1 exerts its effects via receptors before reaching the liver. Indeed, there is accumulating evidence indicating that endogenous GLP-1, similar to CCK, has a paracrine effect on intestinal vagal afferents in rats (Rüttimann et al., 2009; Punjabi et al., 2011).

The secretion of GLP-1 has been studied extensively. It is released postprandially in response to all 3 macronutrients (Feltrin et al., 2004; Pilchiewicz et al., 2007; Ryan et al., 2012). Some studies indicate that carbohydrate is the strongest GLP-1 secretagogue, consistent with its role as an incretin (Elliott et al., 1993; Herrmann et al., 1995; Brubaker and Anini, 2003), but other studies report that lipid and protein also potently stimulate GLP-1 (Feinle et al., 2002; Raben et al., 2003; Feltrin et al., 2004; Blom et al., 2006; Lejeune et al., 2006). As with ghrelin and CCK, lipid hydrolysis is a critical step for GLP-1 secretion. Fatty acids of chain length <12 carbons have little effect (Feltrin et al., 2004; Beglinger et al., 2010).

Depending on the macronutrient, GLP-1 is secreted in a biphasic pattern, with an early-phase secretion within 15 to 30 min after meal onset and a more prolonged second phase from 1 to 3 h postprandially (Herrmann et al., 1995; Schirra et al., 1996; Brubaker and Anini, 2003; Drucker, 2006; Holst, 2007). The GLP-1 response to carbohydrate is rapid and short-lived whereas the responses to lipid and protein are slower and more sustained (Elliott et al., 1993; Schirra et al., 1996; Brubaker and Anini, 2003; Feinle et al., 2003). Several mechanisms have been suggested to control GLP-1 secretion. A neurohumoral “proximal-to-distal loop” may account for the early-phase secretion (Schirra et al., 1996; Brubaker and Anini, 2003) including activation of proximal M1 muscarinic or nicotinic receptors or proximal L-cells that release CCK to stimulate more distal GLP-1 containing L-cells (Anini and Brubaker, 2003; Beglinger et al., 2010). Alternatively, Egan and colleagues (Theodorakis et al., 2006) suggested that after a high-carbohydrate meal, activation of the small number of proximal L-cells may be sufficient to account for the early peak of plasma GLP-1. This is supported by human studies demonstrating that the time courses of glucose-induced GLP-1 secretion and appearance of glucose in the proximal small intestine are similar (Schirra et al., 1996; Theodorakis et al., 2006). However, one of our recent studies underlines the importance of an extended length of small intestine exposed for GLP-1 release (Little et al., 2006), so that during a 60-cm proximal-segment infusion of glucose, plasma GLP-1 concentrations did not change from baseline whereas GLP-1 concentrations increased when glucose was given access to the entire small intestine. Alternatively, the second-phase secretion may also depend on the production of metabolites from unabsorbed nutrients by the gut microflora, most importantly the short-chain fatty acids, acetate, propionate, and butyrate (Delzenne et al., 2010). Another recent hypothesis suggests that bile acids mediate GLP-1 secretion. Parker et al. (2012) and Katsuma et al. (2005) showed in vitro that bile acids induce an increase in GLP-1 by a TGR5 dependent pathway. In addition, Adrian et al. (2010) found that intrarectal infusion of taurouricholic acid increased plasma GLP-1 concentrations in obese and type 2 diabetic
subjects. Others suggested that increases in plasma bile acids may contribute to weight loss and the improvement in glycemic control after RYGB surgery (Nakatani et al., 2009; Patti et al., 2009; Pournaras et al., 2012).

The physiology of GLP-1 secretion has been studied extensively in pigs and appears very similar to that in humans (Holst, 2007). In a widely cited study in pigs, Hansen et al. (1999) estimated that only 25% of the secreted amount reaches the portal circulation and that 40 to 50% of that is destroyed in the liver, so that only 10 to 15% enters the systemic circulation. The GLP-1 agonist liraglutide inhibited eating in obese Göttingen mini-pigs (Raun et al., 2007). We know of no reports that GLP-1 or treatment with a GLP-1 agonist inhibits eating in ruminants although in one study in dairy cows, abomasal infusions of soybean oil led to increased plasma GLP-1 concentrations and decreased DM intake (Relling and Reynolds, 2008), and in another study in sheep, there was a tendency for a reduction in DM intake during 7-d infusions of GLP-1 (Relling et al., 2011).

**PEPTIDE TYROSINE TYROSINE**

Peptide tyrosine tyrosine was first isolated from porcine intestine in 1982 by Tatemoto and named “peptide tyrosine tyrosine” for the tyrosines at each end (Tatemoto, 1982). Peptide tyrosine tyrosine is secreted from endocrine L-cells of the distal ileum and colon, most of which co-express GLP-1 (Adrian et al., 1985, 1987). In humans, about 60% of circulating PYY is PYY(3–36), which results from cleavage of PYY(1–36) by DPPIV (Medeiros and Turner, 1994; Ballantyne, 2006). Peptide tyrosine tyrosine (3–36) is inactivated by nonspecific peptidases (Medeiros and Turner, 1994) and has a half-life in plasma of approximately 9 min (Adrian et al., 1985; Ballantyne, 2006).

In 2002, Batterham et al. (2002) first showed that peripheral infusions of PYY(3–36) that generated postprandial plasma concentrations reduced food intake in humans. They also demonstrated that peripheral and central injections of PYY(3–36) inhibited food intake in rats and mice. Although some researchers could initially not reproduce the eating-inhibitory effect in rodents (Tschop et al., 2004), the anorectic action of PYY(3–36) has now been shown in rats, mice, and other species (Abbott et al., 2005; le Roux et al., 2006; Vrang et al., 2006; Karra et al., 2009). However, it remains unclear whether the anorectic effect of PYY represents a pharmacological or a physiological phenomenon in humans. We evaluated the effect on eating after intravenous infusion of graded doses of PYY(3–36) designed to mimic postprandial PYY secretion (Degen et al., 2005). The results clearly indicated that significant reductions in food intake were present only at plasma concentrations above those after a high-calorie meal. Moreover, nausea was a common side effect, especially at larger doses, indicating that at least some of the effects of PYY on appetite might be due to malaise. Therefore, whether or not PYY has a physiological role in eating control in humans remains to be determined, and studies using specific PYY receptor antagonists will be required to fully characterize its physiological role in eating.

Peptide tyrosine tyrosine (1–36) is thought to exert its effects via at least 3 different neuropeptide Y (NPY)-family receptors (Y1, Y2, and Y5) whereas PYY(3–36) has been shown to be selective for only one, Y2 (Dumont et al., 1995; Ballantyne, 2006). This Y-receptor subtype selectivity is thought to explain the different effects of PYY(1–36) and PYY(3–36) on eating; that is, PYY(1–36) increases eating by binding to orexigenic Y1 and Y5 receptor subtypes whereas PYY(3–36) decreases eating via anorexigenic Y2 receptors (Cummings and Overduin, 2007). Several data are consistent with this hypothesis. For example, Scott et al. (2005) found that Y2 receptor antagonism completely blocked the eating-inhibitory effect of PYY(3–36), and Batterham et al. (2002) showed that PYY(3–36) inhibited eating in wild-type mice but not in Y2-receptor knockout mice. The anorectic action of PYY(3–36) may be mediated by vagal afferents. Receptors for Y2 have been shown to be expressed on vagal fibers, and vagotomy attenuated the anorectic effect of peripheral PYY(3–36; Abbott et al., 2005; Koda et al., 2005). Like GLP-1, PYY may also affect eating via direct effects on gut motility (Witte et al., 2009).

Adrian et al. (1985) first showed in healthy humans that test meals of increasing caloric content caused a dose-related increase in plasma PYY. They also found that lipids caused the greatest increase, protein caused a more moderate increase, and glucose solution caused only a transient and minor release, which has been replicated by several groups (MacIntosh et al., 1999; Essah et al., 2007; Brennan et al., 2012). As with ghrelin, CCK, and GLP-1, PYY secretion depends on lipid hydrolysis and fatty acid chain length ≥12 carbons (Feltrin et al., 2006; Degen et al., 2007).

Plasma concentrations of total PYY or PYY(3–36) increase to an initial peak 15 to 30 min after test meals, reach a second peak approximately 60 to 90 min after meals, and remain increased for up to 6 h (Adrian et al., 1985; Degen et al., 2005; Ballantyne, 2006). As with GLP-1, the secretion of PYY may be stimulated indirectly via duodenally activated neuroendocrine mechanisms or via bile acids as well as by direct contact of nutrients with L-cells (Lin et al., 2000; Ballantyne, 2006). Although the patterns of secretion of PYY and GLP-1 are similar, as expected because both peptides are produced and secreted by L-cells, they are not identical under all conditions. As mentioned previously,
carbohydrates strongly trigger GLP-1 secretion but are weak stimuli for PYY release (Adrian et al., 1985; Herrmann et al., 1995; Brubaker and Anini, 2003), indicating that subpopulations of L-cells may exist that respond differently to a given nutrient stimuli. Indeed, Eissele et al. (1992) found that GLP-1 and PYY were co-expressed in only some enteroendocrine cells in rat, pigs, and humans. Another important consideration in this context is that the patterns of secretion of GLP-1 and PYY do not translate into the same patterns of plasma concentrations of their bioactive forms because DPP IV inactivates GLP-1 but activates PYY (Ballantyne, 2006).

SUMMARY AND CONCLUSIONS

It is increasingly recognized that nutrient stimuli in the GI tract trigger a wide range of changes in GI peptide hormone functions that influence appetite and eating and that these effects are of clinical significance. In particular, the mechanisms controlling the secretion of gut hormones including ghrelin, CCK, GLP-1, and PYY are now thought to be of importance for the success of RYGB surgery in reversing obesity and metabolic disease. In recent years, the use of direct nutrient infusions into different areas of the GI tract and other methods have provided new insights concerning the roles of individual nutrients and specific GI segments in the control of release of these peptides. For example, as reviewed herein, carbohydrates, proteins, and lipids have different potencies as ghrelin, CCK, GLP-1, and PYY secretagogues, and lipid digestion and fatty acid chain length importantly affect their secretagogue potencies. However, it is important to emphasize that elucidating the physiological control of GI peptide secretion is only part of the challenge of understanding the roles of these molecules in eating. As mentioned previously, paracrine as well as endocrine signaling plays an important role in eating control (Geary, 2004; Punjabi et al., 2011). In addition, which aspect of the secretory patterns (e.g., rate of change, specific time window) is critical for effective signal transduction is unknown.

Functional interactions certainly also have a role as, for example, has been convincingly demonstrated for the synergistic effect of gastric fill and CCK on stimulation of vagal afferent activity (Moran and McHugh, 1988; Schwartz et al., 1993). These factors presumably account for the frequent failure to detect correlations between GI peptide concentrations and the amount eaten during single meals (Seimon et al., 2010; Lemmens et al., 2011). In addition, most of the work we reviewed does not consider the effects of these peptides on food reward. It is increasingly recognized that GI nutrient sensing provides positive feedback signals that condition food preferences and stimulate eating (Berthoud, 2011; Sclafani and Ackroff, 2012). Moreover, GI peptides may affect food reward via receptors outside the gut. For example, endocrine GLP-1 may affect GLP-1 receptors in the taste buds to influence the perception of sweet taste (Martin et al., 2009), and a variety of evidence links central ghrelin signaling to food reward (Egecioglu et al., 2010). Emerging data from RYGB surgery also indicate that alterations in GI nutrient sensing produced by the surgery can change the rewarding effects of foods in both rats (Shin et al., 2011) and humans (Miras et al., 2012; Ochner et al., 2012). Finally, these pleiotropic hormones have a variety of other effects as well, such as actions on gastric emptying or glucose metabolism (Ballantyne, 2006; Cummings and Overduin, 2007; Holst, 2007), that may indirectly influence the more direct effect of the hormone on eating.

Our review predominately concerned laboratory rodents and humans. The extent to which these data are relevant to animal husbandry is unclear. The several consistent results across widely divergent mammals indicate that most of the GI mechanisms involved in the control of eating in humans and laboratory rodents are likely to be relevant in agricultural animals. Nevertheless, there are differences (e.g., the effects of central CCK administration in sheep and pigs). Such differences together with the general lack of knowledge concerning the effects of GI peptides on eating in agricultural animals indicate that this area urgently requires further research. Such work seems likely to provide valuable means to improve livestock health and productivity, for example, by adjusting the nutrient composition of feed in ways that optimize GI peptide hormone function.

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Seimon, R. V., K. Lange, T. J. Little, I. M. Brennan, A. N. Pilichiwicz,


