Capromorelin, a ghrelin receptor agonist, increases feed intake and body weight gain in broiler chickens (*Gallus gallus domesticus*)

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ABSTRACT Ghrelin is a hormone that induces orexigenic effects in mammals. However, in avian species, there is scant and conflictive results on the effect of ghrelin on feed intake (**FI**). Therefore, we evaluated the effect of a ghrelin receptor agonist (capromorelin) on FI, ADG, water intake (**WI**), animal behavior and concentrations of ghrelin, glucose, growth hormone (**GH**) and insulin in broiler chickens. One-day-old male broilers were reared as recommended by the industry. At 4 wk of age (experimental day 0; D0), birds were blocked by weight and randomly assigned to 3 treatments in 2 identical trials. Control birds received a vehicle control solution containing 0 mg/kgBW/d of capromorelin. Birds in treatments 2 and 3 received capromorelin at target doses of 6 or 12 mg/kgBW/d of capromorelin (n = 27). FI and WI were measured 3 times a day at 0700 h (Period 1; P1), 1200 h (P2) and 1700 h (P3), while BW was recorded daily. Blood samples were collected on D-1 and D5. Bird behavior (pecking, sitting and standing) was evaluated for 9 h on D2. Data were analyzed using a randomized complete block design with repeated measures over time. Orthogonal polynomial contrasts were used to determine linear and quadratic effects of increasing levels of capromorelin. Polynomial contrasts showed that capromorelin doses linearly increased FI ($P = 0.002$) and ADG ($P = 0.019$). There were no treatment, day or treatment x d interactions on glucose, ghrelin and GH concentrations. However, there was a treatment x d interaction ($P = 0.041$) on insulin concentrations. Concentrations of insulin were higher on D5 for the 0 and 12 mg/kgBW/d treatments as compared with D-1. Polynomial contrasts showed that capromorelin doses linearly increased number of pecks/h ($P = 0.018$). Per hour FI and WI was higher during P1 (i.e., 0700−1200) as compared to P2 and P3 ($P < 0.001$). Our observations suggest that capromorelin linearly increases feed intake; thus, the same effect of that reported in mammalian species.

Key words: ghrelin, capromorelin, feed intake, broiler

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INTRODUCTION

Ghrelin is a short neuropeptide, secreted primarily by the oxyntic cells in the stomach of several species (Kojima et al., 1999). The effect of ghrelin on appetite, glucose homeostasis and energy balance has been reported in mammalian (Vizcarra et al., 2007; Kitazawa et al., 2013), avian (Shousha et al., 2005; Kaiya et al., 2007; Vizcarra et al., 2012) and amphibians (Shimizu et al., 2014) species. In mammals, ghrelin is known to stimulate feed consumption and to promote adipogenesis (Wren et al., 2001; Shimizu et al., 2014). In addition, a rise in ghrelin concentration in plasma has been observed during pre-prandial periods and a decrease after meal consumption (Veedfald et al., 2018). Therefore, in mammalian species, ghrelin is known as an orexigenic hormone (Tschöp et al., 2000; Kaiya et al., 2012; Tsuchiya et al., 2017). However, studies in avian species indicate that appetite is suppressed when ghrelin concentrations in bloodstream are elevated (Saito et al., 2002; Vizcarra et al., 2012). Also, intracerebroventricular (**ICV**) administration of ghrelin inhibits feed intake in birds (Furuse et al., 2001; Saito et al., 2002; Saito et al., 2005) whereas, peripheral administration of ghrelin at different doses have shown controversial results (Shousha et al., 2005; Kaiya et al., 2007; Taofeek et al., 2020). Therefore, the effect of ghrelin in birds seems to be influenced by the route of administration, doses and form of ghrelin used (i.e. acetylated or non-acetylated ghrelin).

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Ghrelin is the natural ligand for the growth hormone secretagogue receptor 1a (**GHSR-1a**). The GHSR-1a belongs to the 7 trans-membrane G protein-coupled receptors family. Activation of the ghrelin receptor is associated with diverse signaling pathways. However, independent ligand levels of inositol phosphate (**IP**) and cAMP-responsive element (**CRE**) demonstrated a high constitutive activity of the GHSR-1a (Holst et al., 2003; Damian et al., 2015). Competition binding experiments have shown a wide range of affinity rates among the different ligands for GHSR-1a, also known as ghrelin agonists, antagonist and inverse agonists. Ghrelin agonist receptors have been widely studied for their pharmacological uses as appetite stimulant in mammalian species. Several ghrelin agonist such as anamorelin, macimorelin, and ibutaren as ligands for GHSR-1a have shown a positive pharmacological effect in the treatment of cancer cachexia and anorexia in mammals, promoting feed intake and regulating energy metabolism (White et al., 2009; Zollers et al., 2017b; Rhodes et al., 2018).

Pecking is a behavioral trait that develops post hatching and is associated with synchronized head movements that are coordinated by visual, olfactory, and tactile cues (Yo et al., 1997). Although many pecks are not associated with ingestion (Yo et al., 1997), feeding behavior has been directly associated to the number of pecks per bird (Gentle et al., 1982; Aydin et al., 2015). Feed intake has been associated with pecking behavior in or around the feeder (Bizeray et al., 2002). Therefore, pecking at feed is an eating behavior used to evaluate feed intake and receptivity to feed quality (Yo et al., 1997; Chagneau et al., 2006). Moreover, the frequency and time spent eating, sitting or standing have been measured as patterns of chicken overall activity (Hocking et al., 1997). The cumulative time for standing and sitting has been useful for the study of normal posture, locomotion, leg disorders, lameness studies, and other physical problems associated to broilers (Weeks et al., 2000; Bokkers and Koene, 2003).

In chickens, the effect of ghrelin receptor agonists on feed intake and animal behavior have not been evaluated. Therefore, the objective of this research was to evaluate the short-term effect of capromorelin on feed intake, body weight gain, water intake, animal behavior and plasmatic concentrations of insulin, glucose, growth hormone and ghrelin in male broiler chickens.

MATERIALS AND METHODS

Animal Rearing and Treatments

One-day-old broiler chickens (*Gallus gallus domesticus*; Ross 708 males) were obtained from a commercial hatchery (n = 60) during 2 different seasons (fall and spring). Birds were placed at random in 2 battery brooders and reared as recommended by industry standards with *ad libitum* feed and water consumption. Birds received a standard corn-soybean-based starter diet from 1 to 19 d of age (22 % CP, 1.0 % Lys, 1.2 % Ca and 0.6 % P) followed by a grower/finisher diet until the end of the experiment (20 % CP, 1.2 % Lys, 1.1 % Ca and 0.6 % P; Purina, MO). Birds were housed at the Poultry Building and exposed to a 23L:1D photoperiod and 22 ± 1.5 °C temperature.

At 3 wk of age (**WOA**), a set of chickens were randomly transferred from the brooders to individual cages (0.6 × 0.5 × 0.5 m) and after 7 d of adaptation to the cages (experimental day 0; D0), animals were blocked by BW and randomly assigned to 3 treatments in 2 identical consecutive trials. Trail 1 was performed during fall and trial 2 was performed during spring for a total of 27 cages. The cage was considered the experiment unit. The criteria used to determine the number of experimental units included a GLMPOWER procedure (SAS, 2019) using data previously obtained in our laboratory (Taofeek et al., 2018). To balance the ethical principles used to justify the minimum number of research animals (Russell and Burch, 1959) and concurrently increase the likelihood of a successful experiment, a stringent a priori power test was used (Demétrio et al., 2013). The number of experimental units was derived by using a power (1-β) of 85% and a probability (α) of 1%.

Entyce (capromorelin), a commercially available FDA-approved ghrelin receptor agonist (FDA, 2016) was used in this experiment (gift of Aratana). Entyce is formulated as an oral solution containing 30 mg/mL of capromorelin. Animals assigned to the control group received 0 mg/kgBW/d (**0 mg**) of capromorelin. Control birds received a vehicle control solution (provided by Aratana) that was dissolved in water. Birds in treatment group 2 and 3 received capromorelin at target doses of 6 mg/kgBW/d **(6 mg)** or 12 mg/kgBW/d **(12 mg)** of capromorelin in water (respectively). The effect of treatments were evaluated during 5 consecutive days (D0-D5). We used 5 experimental days to be consistent with our previous trial using mammalian species (Zollers et al., 2017a). Feed intake **(FI)** and water intake **(WI)** were measured 3 times a day at 0700, 1200, and 1700, whereas BW was recorded daily. Feed and water intake was measured by recording the weight of feed (g) or the volume of water (mL) offered each time minus any unconsumed feed or water remaining. Based on these data (i.e., WI and BW), the medicated water concentration was adjusted daily. To ensure that birds had sufficient medicated water for a 24 h period, the amount of water that was offered to birds per day was calculated based on the amount consumed the previous day times a factor of 1.35. Linear regression was used to calculate ADG.

Blood Samples

Blood samples were collected at 0700 h from the brachial wing on D-1 (1 d before treatments were applied) and at the end of the experiment (D5) using a Saf-T Wing 21 gauge in disposable culture tubes containing EDTA (Fisher Scientific International, PA). In order to inhibit the activation of enzymes, 500 KIU of aprotinin were added per each mL of blood (Fisher Scientific, PA). Tubes

were centrifuged (1,800 × *g* for 15 min at 4°C) within 10 min after collection. After centrifugation, plasma was separated and stored at -80°C for further analyses of glucose (Cayman, MI), chicken growth hormone, chicken insulin and chicken ghrelin (Cosmo Bio USA, CA).

Animal Behavior

Animal behavior associated with feeding (number of pecks/h), sitting (min/h) and standing (min/h) was recorded during 9 consecutive h on D2 (n = 2/trt). A Color CCD video camera was used to record the videos and digitalized using Ethovision XT15 (Noldus et al., 2001). A manual scoring option that integrated pause, rewind and forward choices was used to score start-stop behaviors (sitting and standing) and point events (number of pecks). The videos were watched and analyzed by a human observer as previously described in our laboratory (Vizcarra et al., 2012).

As noted above FI and WI were measured 3 times a day (0700, 1200, and 1700h). Therefore, 3 periods were defined. During Period 1 (0700−1200; **P1**), Period 2 (1200−1700; **P2**) and Period 3 (1700−0700 of the following day; **P3**), feed and water intake were standardized in a per hour basis.

The care, treatments and experimental protocols used were approved by the Institutional Animal Care and Use Committee of Alabama A&M University.

Statistical Analysis

Effects of treatment on BW, FI, WI and hormone concentrations in daily or weekly (5 d) samples were analyzed using a completely randomized block design with repeated measurements over time using PROC GLIMMIX (SAS, 2019). The statistical model initially included the 2 trials (fall and spring). However, the trial effect and its interactions with treatment and time (d) were not significant and data were pooled for analysis. The final model included the effect of treatment (target doses of 0, 6 or 12 mg/kgBW/d of capromorelin), experimental days (D0−D5), blocks, and the treatment x d interactions. The blocks were considered random effects and the treatment and day effect as well as the interactions between these 2 variables were considered fixed effects. Orthogonal polynomial contrasts were used to evaluate linear and quadratic effects for FI, ADG, and number of pecks. The IML procedure (SAS, 2019) was used to generate orthogonal coefficients for unequally spaced contrasts. When appropriate, the BW on D-1 was used as a covariable. Three covariance structures were evaluated (autoregressive, compound symmetry, and ante-dependence). The ante-dependence covariance was selected as the best fit for the data set. Variables associated with FI and WI during the 3 periods (i.e., P1, P2 and P3) were analyzed using repeated measurements over time, whereas, variables associated with number of pecks, standing and sitting on D2 were analyzed using a completely randomized block design. A spearman correlation was used to assess the relationship between concentrations of ghrelin and insulin. Data from animal behavior was analyzed with PROC GLIMMIX (SAS, 2019) using a completely randomized design on D2. Unless otherwise indicated, data is reported as least square means ± SE.

RESULTS

As expected, the actual doses of capromorelin consumed (in drinking water) by birds per day were lower than the target doses (Table 1). Overall, the actual dosage of capromorelin consumed per bird was 78% of the target dose. Nevertheless, the target doses of 0, 6, or 12 mg/kgBW/d of capromorelin are used to identify treatments throughout the manuscript.

There were no significant day or treatment x d interactions on FI and ADG. However, there was a significant treatment effect. Linear orthogonal contrasts best described the relationship between capromorelin doses with FI and ADG (Figure 1). Polynomial contrasts showed that capromorelin doses linearly increased FI ($P = 0.002$) and ADG ($P = 0.019$). Results from linear regressions indicated that there was an increase of 2.7 ± 0.2 g of feed intake per each mg/kgBW of capromorelin added in water. Similarly, there was an increase of 2.0 ± 0.2 g in ADG per each mg/kgBW of capromorelin added in water. There were no significant orthogonal quadratic effect on FI and ADG. There were no day or treatment x d interactions on WI. On average birds consumed 280 ± 39 mL of water/d.

Results from the spearman correlation indicate a positive correlation between ghrelin and insulin in the control group ($P = 0.02$). However, there were no significant correlations between ghrelin and insulin in the 6 and 12 mg/kgBW/d treatments (Table 2). There were no significant treatment, day or treatment x d interactions on ghrelin concentrations. On average concentrations of ghrelin were (103.9 ± 10.0 pg/mL). An interaction between treatment x d was observed ($P = 0.04$) on insulin concentrations (Figure 2). Concentrations of insulin were higher on D5 for the control group (25.0 ± 1.1 μIU/mL) and 12 mg/kgBW/d (24.3

Table 1. Targeted (0, 6, or 12 mg/kgBW/d) and actual doses of capromorelin consumed by broiler chickens (in water).

Target doses (mg/kgBW/d)	Actual intake doses (mg/kgBW/d)					
	D0−D1	D1−D2	D2−D3	D3−D4	D4−D5	Average
6 mg	5.2 ± 0.4	4.5 ± 0.7	4.0 ± 0.97	5.0 ± 0.5	4.6 ± 0.7	4.7 ± 0.3
12 mg	9.7 ± 1.1	9.0 ± 1.5	8.6 ± 1.7	10.3 ± 0.8	9.4 ± 1.3	9.4 ± 0.2

Values represent least square means ± SE of doses of capromorelin (mg) in drinking water over 5 d of treatment.

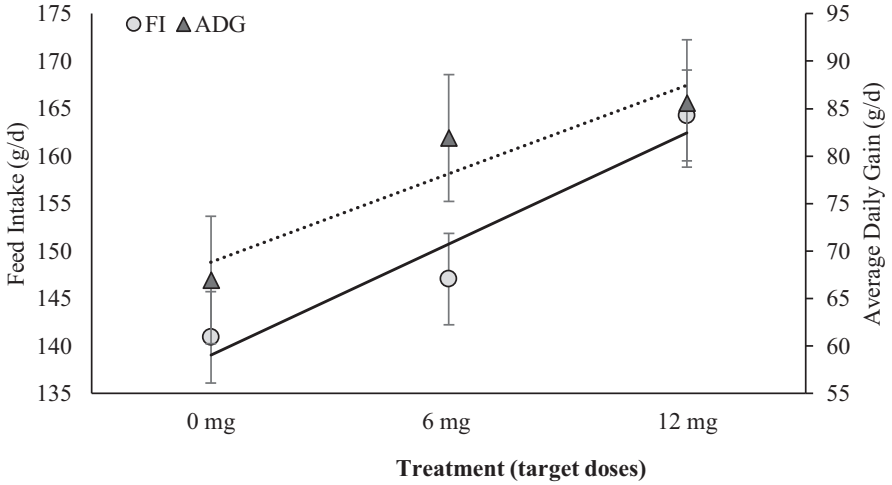

Figure 1. Least squares regressions (lines) and means (symbols) ± SE for feed intake and average daily gain in broiler chickens after administration of different target doses of capromorelin (0, 6, or 12 mg/kgBW/d) in water during 5 experimental days (D0−D5). There was a linear orthogonal effect of treatments on feed intake FI ($P = 0.002$) and ADG ($P = 0.019$).

Table 2. Spearman correlation coefficients (r^2) for the relationship between ghrelin and insulin concentrations at target doses of 0, 6, and 12 mg/kgBW/d of capromorelin in broiler chickens.

Treatments (target doses)	r^2	$P=$
0 mg	0.60	0.02
6 mg	-0.08	0.74
12 mg	0.02	0.94

± 1.1 μIU/mL) as compared with D-1 (20.9 ± 1.1 μIU/mL and 22.5 ±1.1 μIU/mL for control and 12 mg/kgBW/d, respectively).

There were no significant treatment, day or treatment x d interactions for glucose and GH concentrations. On average concentration of glucose and GH were 230 ± 12 mg/dL and 9.6 ± 1.8 ng/mL (respectively)

Animal Behavior

There was a significant treatment effect on the number of pecks/h (Figure 3). Polynomial contrasts showed that capromorelin doses linearly increased the number of pecks/h ($P = 0.018$). Results from linear regression analysis indicated that there was an increase of 15.9 ± 0.6 pecks/h per each mg/kgBW of capromorelin added in water. When behavioral data was evaluated relative to periods, there were no significant treatment or treatment x d effects. However, WI was higher during P1 (24.3 ± 1.9 mL/h) as compared to P2 (14.5 ± 1.9 mL/h) and P3 (8.9 ± 1.9 mL/h) ($P < 0.001$). Likewise, on average birds increased feed consumption/h on P1 (13.9 ± 0.9 g/h) as compared with P2 (7.8 ± 0.9 g/h) and P3 (4.4 ± 0.9 g/h) (Figure 4). There were no significant differences on standing and sitting time between treatments.

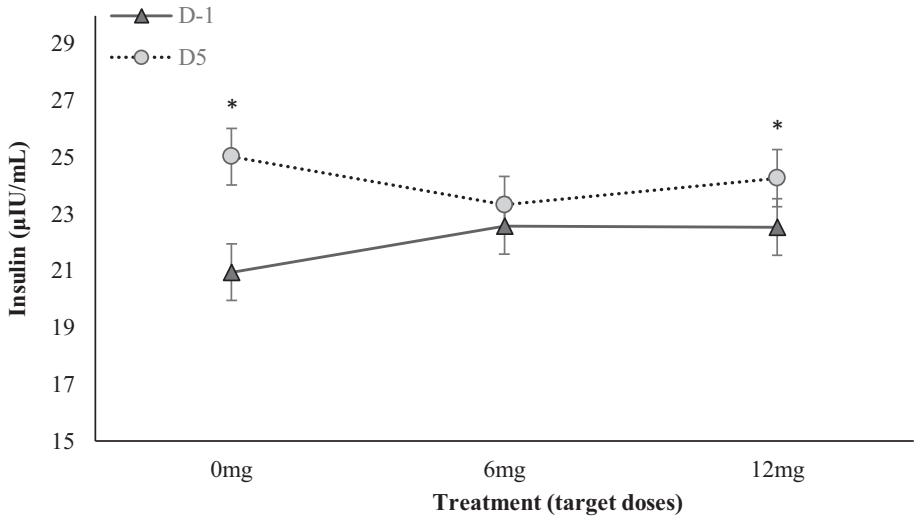

Figure 2. Least square means ± SE for insulin concentrations (μIU/mL) in broiler chickens before (D-1) and after (D5) administration of target capromorelin doses (0, 6, or 12 mg/kgBW/d) in water. There was a significant treatment x d interaction. *= significant differences between days ($P < 0.1$).

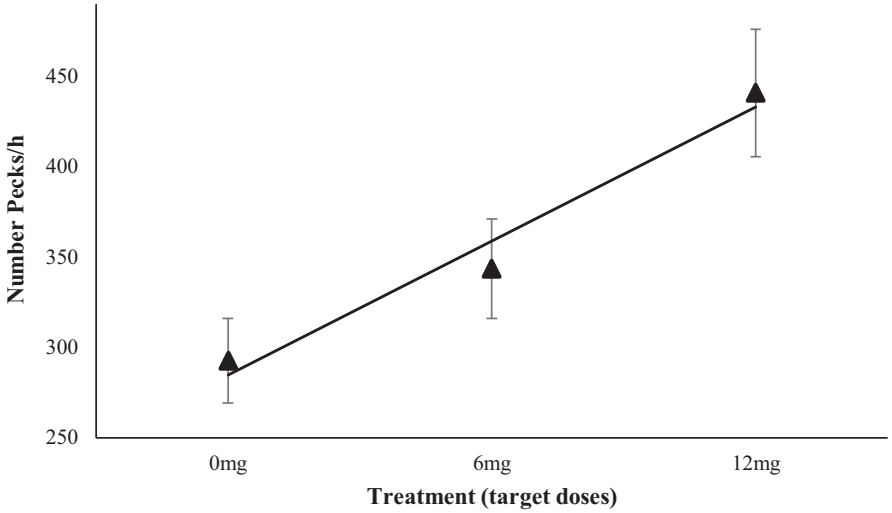

Figure 3. Least squares regressions (lines) and means (symbols) ± SE for number of pecks/h in broiler chickens on experimental D2. Birds were administered target doses of capromorelin (0, 6, or 12 mg/kgBW/d) in water. There was a liner orthogonal effect of treatments on number of pecks ($P = 0.018$).

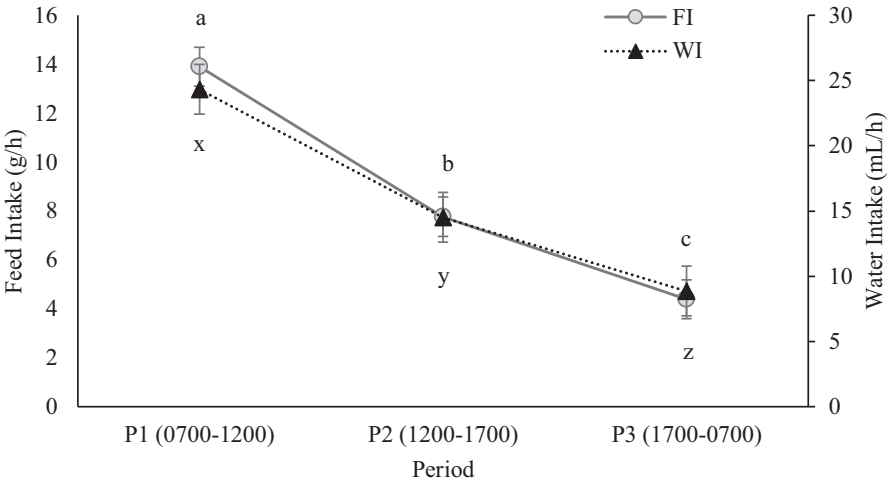

Figure 4. Least squares means ± SE for feed intake and water intake per period in broiler chickens. Feed and water intake were measured 3 times a day (0700, 1200, and 1700 h). During Period 1 (0700−1200; P1), Period 2 (1200−1700; P2) and Period 3 (1700−0700 of the following day; P3), feed and water intake were standardized in a per h basis. Different letters represent differences ($P < 0.01$) in feed^{abc} and water^{xyz} intake between periods.

DISCUSSION

Linear dose-dependent increase of capromorelin on feed intake, body weight gain and number of pecks reflects the orexigenic effect of ghrelin in male broiler chickens. These results are in agreement with findings of Zollers et al. (2017a), who reported that dogs with anorexia, hyporexia and dysrexia receiving a dose of 3mg/kgBW/d of capromorelin for 4 consecutive days significantly increased feed intake and body weight. Also, Shousha et al. (2005) described an increase in feed consumption in Japanese quails after intraperitoneal (IP) injections of ghrelin. We have also reported that intravenous (IV) infusion of different dose/frequency combinations (0, 0.5, 1, 4 nM/100g BW/d of acyl-ghrelin in pulse every 2 h) and a continuous infusion of 1 nM/100g BW/d of acyl-ghrelin decreased FI whereas infusion of des-acyl-ghrelin increased feed intake (Taofeek et al., 2020). It is well recognized that the acyl-modification of ghrelin is necessary for the activation of the GHSR-1a receptor, whereas the affinity of des-acyl-ghrelin to GHSR-1a is very low (Shiimura et al., 2020). However, a GHSR-1a-independent des-acyl-ghrelin function that exhibits physiologic effects have been reported in several laboratories (Toshinai et al., 2006; Heppner et al., 2014; Zhang et al., 2017). Thus, des-acyl ghrelin may regulate feed intake, independently from acyl-ghrelin, after binding to a still unknown cognate receptor.

In neonatal chicks, ICV injections of ghrelin at doses of 0.1 to 3.2 nM resulted in a significant decrease of feed intake (Saito et al., 2002). Similar results were observed when a ghrelin agonist, GHRP-6, was centrally administered in 3-day-old chicks (Khan et al., 2006). In addition, previous studies in our laboratory showed an increase in FI and peck rate in turkeys passively

immunized against ghrelin (Vizcarra et al., 2012) as opposed to decreased FI in actively immunized mammals (Vizcarra et al., 2007).

The differential form of action of ghrelin in mammalian and avian species is thought to be associated with the activation of different neurons in the hypothalamus. Binding of acyl-ghrelin to the GHSR-1a receptor triggers the protein kinase A (**PKA**) signaling-pathway that leads to phosphorylation of AMP-activated protein kinase (**AMPK**). In turn, activation of AMPK in the hypothalamus is associated with increased feed intake (Minokoshi et al., 2004). Therefore, changes in the modulation of AMPK regulates the expression of anorexigenic or orexigenic signals. In mammals, ghrelin increased phosphorylation of AMPK and thereby stimulated the expression of the orexigenic neuropeptide Y and agouti-related protein (**AgRP**) in the arcuate nucleus (**ARC**) of the hypothalamus (Tschöp et al., 2000; Kola and Korbonits, 2009). However, in chickens, genetic selection seems to have altered the hypothalamic signaling of AMPK. Infusion (ICV) of ghrelin in chickens downregulates AMPK and thereby decreases appetite (Xu et al., 2011). The effect of ghrelin on feed intake in birds is also thought to be associated with the activation of neurons expressing the anorexigenic corticotropin-releasing hormone (CRH). Suppression of feed intake in chickens was induced by ICV injections of ghrelin, but it was attenuated by co-injection of a CRH receptor antagonist (Saito et al., 2005). However, ICV injections of a CRH-like peptide (Urocortin-3; UCN-3) but not CRH increased plasma ghrelin concentration in chickens (Khan et al., 2014). Since UCN-3 has more affinity to the CRH type 2 receptor (Telegdy and Adamik, 2008), the effect of ghrelin on feed intake may be mediated by the CRH system and the 2 receptors present in the CRH family. Other line of research in chickens have found that ICV infusion of beta-melanocyte-stimulating hormone decrease the expression of ghrelin in the hypothalamus but increases the expression of the receptor (Cao et al., 2020) suggesting that other factors, such as pro-opiomelanocortin, are also involved. Additionally, the GHSR-1a receptor exhibits a highly constitutive activity (Holst et al., 2003). Consequently, the ability of the ghrelin receptor to retain certain degree of activity independently of the ligand may also play a role in the differential regulation of ghrelin in feed intake. Taken together, the neuroendocrine mechanism by which ghrelin differentially regulates feed intake in avian species has not yet been fully understood.

The wide distribution of ghrelin and GHSR-1a in mammals and non-mammals suggests a multifunctional action of the hormone that also includes paracrine and autocrine effects (Kaiya et al., 2009). For instance, the expression of GHSR-1a has been reported in the solitary nucleus, which receives afferents from baroreceptors and exert an important function in the control of blood pressure (Perello et al., 2018). An increase in blood pressure tend to cause an anti-dipsogenic effect in mammals (Hashimoto et al., 2007). In rats, water consumption significantly decreases after peripheral (IV) and central (ICV) administration of ghrelin. This reduction in water consumption has been attributed to stimulated expression of FOS in the area postrema and the solitary nucleus (Hashimoto et al., 2007). Similarly, the anti-dipsogenic effect of ghrelin was also observed in neonatal chicks subjected to ICV doses of 0.01 nM of ghrelin (Tachibana et al., 2006). In the present experiment, oral administration of capromorelin did not affect water consumption, suggesting that the ghrelin receptor agonist might not have an antidipsogenic effect in broiler chickens.

A cross-path communication between ghrelin and insulin pathways explains the influence of ghrelin on energy metabolism. In agreement to our results in control birds, it has been reported a correlation between ghrelin and insulin in mammalian (Haqq et al., 2003; Dezaki, 2013; Korek et al., 2013) and avian species (Song et al., 2019). However, there was no correlation between ghrelin and insulin in birds treated with 6 and 12 mg/kgBW/d of capromorelin. The lack of association between insulin and ghrelin in treated (6 mg and 12 mg birds) may reflect a much higher complexity of secondary effects of increased insulin secretion and potential up- or down-regulation of ghrelin receptors in broilers (Shiraishi et al., 2011). On the other hand, partial or full agonists are design to have a higher affinity for the receptor than the natural ligand. Thus, the action of an agonist depends on the concentrations required to have half-maximal biological response (Carpino, 2005). As noted above, GHSR-1a is constitutively active (Holst et al., 2003). Therefore, ghrelin agonists tend to present a lower binding affinity as compare with endogenous ghrelin, which might explain the lack of correlation between insulin and ghrelin (Holst et al., 2003; Callaghan and Furness, 2014). Although insulin concentrations were higher on D5 for the control and 12 mg/kgBW/d treatment groups, glucose concentrations were not affected by treatments. It is well recognized that broilers have higher blood glucose concentration than mammals and that large doses of insulin are required to stimulate glucose uptake in insulin responsive tissues in chickens. Therefore, the lack of response to glucose observed in the present experiment could be explained by the characteristic insulin-resistance reported in chickens (Langslow et al., 1970).

In contrast with the results in dogs (Zollers et al., 2017a), treatments in the present experiment failed to affect endogenous concentrations of GH. In the present experiment, birds had constant access to capromorelin doses in water whereas; dogs received a single bolus treatment. Based on results of WI, birds drunk less water during P3 (1700−0700) therefore the intake of capromorelin was decreased. Since blood samples were obtained at 0700 h we can only speculate that the lack of response to GH might be associated with decreased capromorelin consumption at the time the blood samples were collected. Further studies evaluating insulin and GH at different times are needed to understand capromorelin short-term changes on energy metabolism hormones.

Animal Behavior

In the present study, we found a linear dose response between the number of pecks and capromorelin doses. In addition, we found that FI and WI were increased on P1 as compared with P2 and P3. Similar results were observed by Hocking et al. (1997), who reported a higher feed consumption in broilers during the morning than in the afternoon. However, behavior associated with sitting and standing time was not significant affected by treatments or periods. Eating, drinking and walking behaviors are increased in the morning time in broilers (Bayram and Özkan, 2010). The discrepancies with our results might be explained for the potential effects of other factors such as body weight, age, feed quality, feed particle size and photoperiod (Yo et al., 1997; Weeks et al., 2000).

In conclusion, our data clearly demonstrates the orexigenic effect of oral administration of capromorelin in broiler breeders. Birds subjected to higher doses of capromorelin consumed on average 16.6% more feed and gained 18.8% more weight than control birds; thus, the same effect of that reported in mammalian species.

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DISCLOSURES

The authors declare no conflicts of interest.

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