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Role of Central Cannabinoidergic System on Ghrelin-Induced Hypophagia in Layer-Type Neonatal Chicken

Mohammadreza Taherian[1], Morteza Zendehdel[2], Shahin Hassanpour[3]

[1]Department o f Animal Sciences, Faculty of Agriculture, Kashmar Branch, Islamic Azad University, Kashmar, Iran

[2]Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tehran, Tehran, Iran

[3]Department of Basic Sciences, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran

Abstract:

BACKGROUND: Feeding behavior is regulated via a complex network which interacts through diverse signals from central and peripheral tissues.

OBJECTIVES: The main purpose of the current study was to determine the role of central cannabinoidergic (CBergic) system on ghrelin-induced hypophagia in 3-h food deprived (FD3) neonatal chicken.

METHODS: In experiment 1, chicks were ICV injected with control solution, ghrelin (0.6 nmol), SR141716A (selective CB1 receptors antagonist, 6.25 µg) and ghrelin + SR141716A. In experiment 2, chickens received ICV injection of (A) control solution, ghrelin (0.6 nmol), AM630 (selective CB2 receptors antagonist, 1.25 µg) and ghrelin + AM630. In experiment 3, chickens were ICV injected with control solution, 2-AG (selective CB1 receptors agonist, 2µg), GSK1614343 (selective ghrelin receptors antagonist, 6 nmol) and 2-AG + GSK1614343. In experiment 4, the birds received control solution, CB65 (selective CB2 receptors agonist, 6.25 µg), CB65 + GSK1614343. Then the cumulative food intake was measured until 120 min post injection.

RESULTS: According to the results, ICV injection of the ghrelin, significantly decreased cumulative food intake ($P<0.05$). Co-injection of the ghrelin + SR141716A and/or ghrelin + AM630 significantly amplified ghrelin-induced hypophagia compared to control group ($P<0.05$). Hyperphagia observed by ICV injection of the 2-AG (2 µg) ($P<0.05$). Co-injection of the 2-AG + GSK1614343 increased food intake compared to control group ($P<0.05$). ICV injection of the CB65 (1.25 µg) significantly increased food intake ($P<0.05$). Also, co-injection of the CB65 + GSK1614343 significantly amplified cumulative food intake in FD3 neonatal layer-type chicken ($P<0.05$).

CONCLUSIONS: These results suggested ghrelin-induced hypophagia mediates via CB1 and CB2 receptors in neonatal layer-type chicken.

Keywords:

Cannabinoid, Central food intake, Ghrelin, Neonatal layer-type chicken

Correspondence

Shahin Hassanpour, Department of Basic Sciences, Faculty of Veterinary Medicine, Science and Research Branch, Islamic Azad University, Tehran, Iran

Tel: +98(21) 44868560, Fax: +98(21) 44865179, Email: hassanpour.shahin@gmail.com

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Introduction

Food intake and energy expenditure as a complex phenomenon is regulated by a complex neural system from central and peripheral signals (Skibicka et al. 2013). Based on neurobiological reports, gut–brain peptides such as ghrelin have regulatory role on appetite and reward (Engel et al. 2015) which in mammalian ghrelin is the only orexigenic hormone identified to date (Kalafateli et al. 2018). Circulating hormone ghrelin and the neural circuits in the central nervous system (CNS) have an important role in appetite control (Cardona Cano et al. 2012). Avian ghrelin is a 26-amino acid peptide which is identified in the stomach, brain and abdominal fat (Pingwen et al. 2011). Ghrelin has 3 subtypes of ghrelin receptors including S-R1a, GHS-R1aV (homologous to mammalian GHS-R1b) and GHS-R1tv which have been identified in broilers. Ghrelin provokes release of growth hormone through GH secretagogue receptors (GHS-R) (Engel et al. 2015). Systemic or Intracerebroventricular (ICV) injection of the ghrelin increases food intake in rat (Kaiya et al. 2013) while ghrelin inhibits feed intake in broiler (Saito et al. 2005; Zendehdel et al. 2012) and Japanese quail (Kitazawa et al. 2017). It has regulatory role on the mesolimbic reward system including ventral tegmental area (VTA) and the nucleus accumbens (NAc) which are involved in hedonic feeding (Skibicka et al. 2013).

The endocannabinoids (ECBs) have two receptors (CB1 and CB2). CB1 are receptors expressed abundantly in the CNS while CB2 receptors are identified in the peripheral nervous system (PNS), immune cells and tissues (Hassanpour et al. 2015). ICV injection of the CB agonists stimulated food intake in rodents while SR141716A (selective CB1 receptors antagonist) decreased food consumption in rat (Ierucka-Rybak et al. 2016). ICV administration of 2-AG (CB1 cannabinoid receptors agonist, 1 μg) or JWH015 (CB2 cannabinoid receptors agonist, 25 μg) amplified food intake in neonatal layer type chicken (Alizadeh et al. 2015) while CB2 receptors have orexigenic role in neonatal broilers (Emadi et al. 2011). However, Novoseletsky et al. (2011) reported intravenous injection of AM251 (inverse CB1 receptors agonist) leads to transient attenuation on food intake in meat-type chicken. Despite more than two decades passing from ghrelin discovery, its interaction with other neurotransmitters is not fully clarified yet (Zendehdel and Hassanpour, 2014). It is assumed an interaction exists between central ghrelin with other neurotransmitters such as dopamine (Skibicka et al. 2012), glutamate (Fuente-Martín et al. 2016) and CBergic systems. It is reported ICV injection of the CB receptor antagonist attenuates ghrelin-induced activation of the mesolimbic dopamine system in mice (Kalafateli et al. 2018). Ghrelin elevates hypothalamic ECB content in wild-type mice, but not in CB1 KO or rimonabant-treated mice (Lim et al. 2013). Additionally, CBs require the ghrelin receptor on ghrelin-induced cellular energy metabolism (Lim et al. 2013). So far, several researches have been done to determine central food intake regulation in both avian and mammalians but these regulatory systems are not similar among them. For instance, in rodents, ghrelin has orexigenic effect (Kaiya et al. 2011) while it has anorexigenic role in domestic fowls (Saito et al. 2005; Zendehdel and Hassanpour 2014).

Therefore, the possible contribution of central ghrelin and CBergic system on food intake regulation will be employed in the layer industry to enhance hen's productivity by manipulating appetite and lessening malnutrition concerns. So, the aim of the current study was to determine interaction of central CBergic system on ghrelin-induced hypophagia in neonatal layer-type chicken.

Material and Methods

Animals: A total of 176 one-day-old layer-type chickens (Hy-line) were purchased from a local hatchery. At 2 days of age, birds were randomly transferred to individual cages and kept at a temperature of 30 ± 1 ºC with 50 ± 2 percent humidity (Olanrewaju et al. 2017). Birds were housed according to a completely randomized design. During the study birds had ad libitum access to fresh water and a starter diet containing 21% crude protein and 2850 kcal/kg of metabolizable energy (Animal Science Research Institute Co., Iran) (table). Three hours prior to the injections, birds were food deprived (FD3) but had free access to water. Animal handling and experimental procedures were performed according to the Guide for the Care and Use of Laboratory Animals by the National Institutes of Health (USA) and the current laws of the Iranian government for animal care.

Experimental Drugs: Drugs include ghrelin, SR141716A (a selective CB1 receptors antagonist), AM630 (a selective CB2 receptors antagonist), GSK1614343 (selective ghrelin receptors antagonist), 2-AG (2-Arachidonoylglycerol, a selective CB1 receptors agonist), CB65 (a selective CB2 receptors agonist) and Evans blue were purchased from Sigma Co. (Sigma, USA) and Tocris Co. (UK). Drugs except 2-AG were first dissolved in absolute dimethyl sulfoxide (DMSO) then diluted with 0.85% saline containing Evans blue at a ratio of 1/250. DMSO with this ratio does not have cytotoxic effect (Qi et al. 2008).

ICV injection procedures: In this study, 4 experiments designed to investigate interconnection of CBergic system with ghrelin on cumulative food intake in neonatal meat-type birds (each experiment includes 4 groups within 11 replicates in each group). Prior to each experiment, the chicks were weighed and based on their body weight divided into experimental groups so the average weight between treatment groups was as uniform as possible. ICV injection was applied using a microsyringe (Hamilton, Switzerland) without anesthesia according to the technique previously described by Davis et al. (1979) and Furuse et al. (1997) in which head of the birds was held with an acrylic device while the bill holder was 45º and calvarium parallel to the surface of table (Van Tienhoven and Juhasz, 1962). A hole was drilled in a plate in which the skull over the right lateral ventricle was immediately overlaid through this plate. A microsyringe was inserted into the right ventricle via the hole and tip of the needle penetrated 4 mm beneath the skin of the skull. It is revealed that, there is no injection-induced physiological stress using this method in neonatal chicks (Saito et al. 2005). Each chick received an ICV injection (with vehicle or drug solution) in a volume of 10 µL (Furuse et al. 1999). The control group received control solution (saline containing Evan's blue 10 µL) (Furuse et al. 1999). Right away after injection, FD3 birds were returned to their individual cages and were supplied with fresh water and food (preweighed). Food consumption was calcu-

lated as a percentage of body weight (BW) (g/100g BW) to minimize impact of body weight on the amount of food intake. Each bird was used just once in each experimental group. At the end of the experiments, accuracy of placement of the injection in the ventricle was verified by presence of Evans blue followed by slicing the frozen brain tissue. All experimental procedures were done from 8:00 until 15:30.

Feeding experiments: In experiment 1, four groups of FD3 chicks received a dose of either the ICV injection of (A) control solution, (B) ghrelin (0.6 nmol), (C) SR141716A (6.25 µg) and (D) ghrelin + SR141716A. In experiment 2, FD3 chickens received ICV injections as follows: (A) control solution, (B) ghrelin (0.6 nmol), (C) AM630 (1.25 µg) and ghrelin + AM630. In experiment 3, fasted chickens were ICV injected with (A) control solution, (B) 2-AG (2µg), (C) GSK1614343 (6 nmol) and (D) 2-AG + GSK1614343. In experiment 4, the birds received (A) control solution, (B) CB65 (6.25 µg), (C) GSK1614343 (6 nmol) and (D) CB65 + GSK1614343. These doses of drugs were determined according to the previous and our pilot studies (Emadi et al. 2011; Novoseletsky et al. 2011; Zendehdel and Hassanpour, 2014).

Statistical analysis: Data is presented as mean ± SEM (standard error of the mean). Cumulative food intake (as percent of body weight) was analyzed by repeated measure two-way analysis of variance (ANOVA) using SPSS 16.0 for Windows (SPSS, Inc., Chicago, IL, USA). For treatment showing a main effect by ANOVA, means were compared by Tukey-Kramer test. $P<0.05$ was considered as significant difference between treatments.

Results

Effect of ICV injection of ghrelin, CB1 receptors antagonist and their combination on cumulative food intake in neonatal chickens is presnted in Fig. 1. According to the results, ICV injection of the effective dose of the ghrelin, significantly decreased cumulative food intake in FD3 compared to control group ($P<0.05$). ICV injection of sub effective dose of the SR141716A (6.25 µg) had no significant effect on food intake in FD3 birds ($P>0.05$). Co-injection of the ghrelin + SR141716A significantly amplified ghrelin-induced hypophagia compared to control group ($P<0.05$) (Fig. 1).

Effect of ICV injection of ghrelin, CB2 receptors antagonist and their combination on cumulative food intake in neonatal chickens is shown in Fig. 2. ICV injection of the effective dose of the ghrelin, significantly decreased cumulative food intake in FD3 compared to control group ($P<0.05$). ICV injection of the sub effective dose of the AM630 (1.25 µg) had no significant effect on food intake in FD3 birds ($P>0.05$). Co-injection of the ghrelin + AM630 significantly amplified hypophagic effect of the ghrelin compared to control group ($P<0.05$) (Fig. 2).

Effect of ICV injection of selective ghrelin receptors antagonist, CB1 receptors agonist and their combination on cumulative food intake in neonatal chickens is presented in Fig. 1. Hyperphagia is observed by ICV injection of the 2-AG (2 µg) ($P<0.05$). ICV injection of the GSK1614343 (6 nmol) had no effect on cumulative food intake in FD3 neonatal layer-type chicken ($P>0.05$). Co-injection of the 2-AG + GSK1614343 increased food intake compared to control group ($P<0.05$) (Fig. 3).

Table 1. Ingredient and nutrient analysis of experimental diet. ME: metabolisable energy, CP: crude protein, per kg of diet, the mineral supplement contains 35.2 g manganese from MnSO4·H2O; 22 g iron from FeSO4·H2O; 35.2 g zinc from ZnO; 4.4 g copper from CuSO4·5H2O; 0.68 g iodine from ethylene diamine dihydroiodide; 0.12 g seleniumfrom Na2SeO3. The vitamin supplement contains 1.188 g of retinyl acetate, 0.033 g of dl-α-tocopheryl acetate, 8.84 g of tocopherol, 1.32 g of menadione, 0.88 g of thiamine, 2.64 g of riboflavin, 13.2 g of nicotinic acid, 4.4 g of pantothenic acid, 1.76 g of pyridoxin, 0.022 g of biotin, 0.36 g of folic acid, 1500 mg of choline chloride.

Ingredient	(%)	Nutrient analysis	
Corn	52.85	ME, kcal/g	2850
Soybean meal, 48% CP	31.57	Crude protein (%)	21
Wheat	5	Linoleic acid (%)	1.69
Gluten meal, 61% CP	2.50	Crude fiber (%)	3.55
Wheat bran	2.47	Calcium (%)	1
Di-calcium phosphate	1.92	Available phosphorus (%)	0. 5
Oyster shell	1.23	Sodium (%)	0.15
Soybean oil	1.00	Potassium (%)	0.96
Mineral premix	0.25	Chlorine (%)	0.17
Vitamin premix	0.25	Choline (%)	1.30
Sodium bicarbonate	0.21	Arginine (%)	1.14
Sodium chloride	0.20	Isoleucine (%)	0.73
Acidifier	0.15	Lysine (%)	1.21
DL-Methionine	0.10	Methionine (%)	0.49
Toxin binder	0.10	Methionine + cystine (%)	0.83
L-Lysine HCl	0.05	Threonine (%)	0.70
Vitamin D3	0.1	Tryptophan (%)	0.20
Multi enzyme	0.05	Valine (%)	0.78

Effect of ICV injection of selective ghrelin receptors antagonist, CB2 receptors agonist and their combination on cumulative food intake in neonatal chickens is shown in Fig. 4. ICV injection of the CB65 (1.25 µg) significantly increased food intake in comparison to the control group (P<0.05). ICV injection GSK1614343 (6 nmol) as sub effective dose, had no effect on feeding behavior in FD3 neonatal layer-type chicken (P>0.05). However, co-injection of the CB65 + GSK1614343 significantly amplified cumulative food intake in FD3 neonatal layer-type chicken (P<0.05) (Fig. 4).

Discussion

To the best of our knowledge, this is the first report on interaction of central CBergic system on ghrelin-induced hypophagia in neonatal layer-type chicken. Based on the results, ICV injection of the ghrelin significantly decreased cumulative food intake in FD3 neonatal layer-type chicken. ICV injection of the ghrelin decreases food intake in neonatal chicks (Saito et al. 2005). ICV injection of ghrelin (0.3, 1.1, 4.3 and 6.2 nMol) decreased food intake in 8-week-old broilers (Müller et al. 2015). ICV injection of the ghrelin (1 nMol) decreased food intake in Japanese quail (Kitazawa et al. 2017). ICV injection of the ghrelin increases food intake in laboratory animals (Kaiya et al. 2013). Injection of ghrelin increased in dopamine β- hydroxylase expression in nucleus tractus solitarious (NTS) (Date et al. 2006). The role of ghrelin is completely different among avian and mammalian. It is an orexigenic peptide in mammalian while

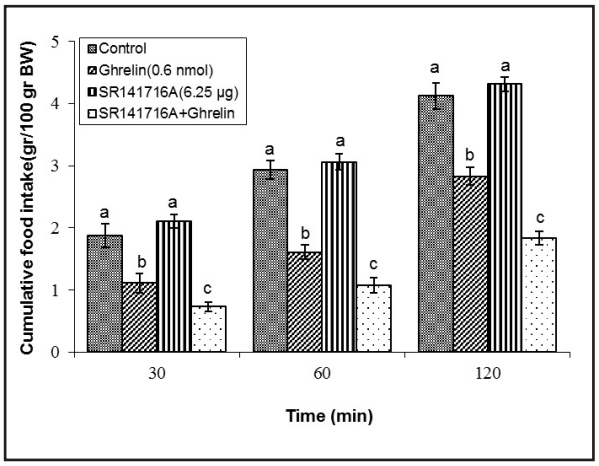

Figure 1. Effect of ICV injection of SR141716A (6.25 µg), ghrelin (0.6 nmol), and their combination on cumulative food intake (% BW) in neonatal chickens. SR141716A: selective CB1 receptors antagonist. There are significant differences between groups with different superscripts in a column (a, b and c; $P< 0.05$).

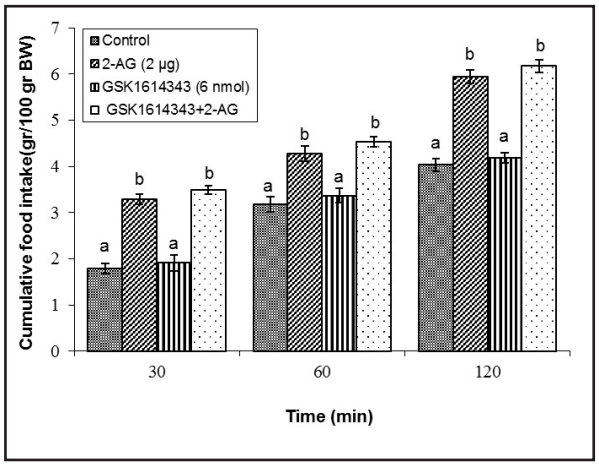

Figure 2. Effect of ICV injection of AM630 (1.25 µg), ghrelin (0.6 nmol), and their combination on cumulative food intake (% BW) in neonatal chickens. AM630: selective CB2 receptors antagonist. There are significant differences between groups with different superscripts in a column (a, b and c; $P< 0.05$).

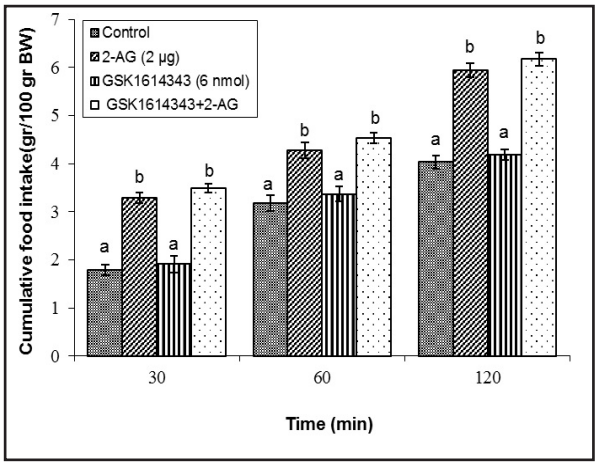

Figure 3. Effect of ICV injection of GSK1614343 (6 nmol), 2-AG (2 µg) and their combination on cumulative food intake (% BW) in neonatal chickens. GSK1614343: selective ghrelin receptors antagonist. 2-AG: CB1 receptors agonist. There are significant differences between groups with different superscripts in a column (a and b; $P< 0.05$).

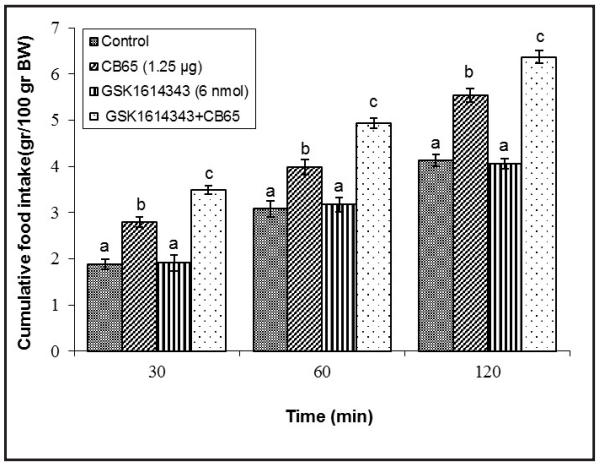

Figure 4. Effect of ICV injection of GSK1614343 (6 nmol), CB65 (1.25 µg) and their combination on cumulative food intake (% BW) in neonatal chickens. GSK1614343: selective ghrelin receptors antagonist. CB65: CB2 receptors agonist. There are significant differences between groups with different superscripts in a column (a, b and c; $P< 0.05$).

it is known as an anorexigenic neurotransmitter in chicken (Saito et al. 2005; Zendehdel and Hassanpour, 2014). In mammals, ghrelin-induced hyperphagia mediates via activating neuropeptide Y (NPY) and agouti-related protein (AgRP) neurons. Ghrelin receptors are highly expressed in NPY than pro-opiomelanocortin (POMC) neurons in rat brain (Kaiya et al. 2013). Given the estimated 300 million years of evolutionary distance between mammals and avian, it is not surprising the discrepancy has been found in the central food intake and energy expenditure regulation (Novoseletsky et al. 2011).

According to the results, hyperphagia observed by ICV injection of the CB1 and CB2 receptors agonists, 2-AG and CB65,

respectively which was similar to mammals (Wiley et al. 2012; Ierucka-Rybak et al. 2016; Androvicova et al. 2017). However, the inconsistency between broiler and layers might be related to the differences in localization, affinity or expression of CB1 receptors (Emadi et al. 2011; Novoseletsky et al. 2011). Although CB2 receptors are primarily expressed in the cells and organs of the immune system, CB2-like protein has been isolated in the brain of neonatal chicks and disappears in adult chickens (Breivogel et al. 2018). CB receptors impress orexigenic effect by stimulation of NPY and blocking of the POMC neurons in the arcuate nucleus (D'Addario et al. 2014).

As observed, co-injection of the ghrelin + CB1 receptors antagonist amplified ghrelin-induced hypophagia. Co-injection of the ghrelin + CB2 receptors antagonist amplified hypophagic effect of the ghrelin. Co-injection of the CB1 receptors agonists + selective ghrelin receptors antagonist (GSK1614343) increased food intake. Also, co-injection of the CB2 receptors agonists + GSK1614343 amplified cumulative food intake in FD3 neonatal layer-type chicken. In a study, Senin et al. (2013) reported peripheral blockade of the CB1 receptor decreased food intake in food-deprived rat. This anorexigenic effect is likely a consequence of decreases in gastric ghrelin secretion. It is suggested CB1 receptor-mediated mechanism influences gastric ghrelin secretion and feeding behavior via mTOR pathway (Senin et al. 2013). In CB1-knockout mice ghrelin had no orexigenic effect. Pharmacological blockade of CB1 receptors inhibit signaling of the ghrelin on hypothalamic AMP-activated protein kinase (AMPK) activity (Lim et al. 2013). Ghrelin inhibits excitatory inputs of the CB1 receptors on the paraventricular nucleus (PVN) and this effect is abolished by ICV injection of CB1 antagonist in mice (Lim et al. 2013). So, CBergic signaling pathway is necessary for stimulatory effects of ghrelin on AMPK activity and food intake (Lim et al. 2013). Ghrelin exerts its hypothalamic effects via growth hormone secretagogue receptor type-1 and perhaps other receptors using this pathway to stimulate ECBS synthesis. Stimulatory effect of ghrelin on 2-AG blocked by rimonabant administration in mice. So, it seems interconnection exists between central CBergic and ghrelin neurons on food intake (Lim et al. 2013). In conclusion, these results suggested ghrelin-induced hypophagia mediates via CB1 and CB2 receptors in neonatal layer-type chicken. However, merit studies have been done on interaction of the ghrelin and CBergic in lab animal model but scarce information is present on interaction of the neurotransmitters on feeding behavior in avian. Further researches are needed to determine cellular and molecular mechanism(s) involved in interaction of the CB receptors on ghrelin-induced hypophagia in FD3 chicken.

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Conflicts of interest

The author declared no conflict of interest.

References

Alizadeh, A., Zendehdel, M., Bababpour, V., Charkhkar, S., Hassanpour, S. (2015). Role of cannabinoidergic system on food intake in neonatal layer-type chicken. Vet Res Com-

mun, 39, 151–157. https://doi.org/10.1007/s11259-015-9636-3 PMID: 25902906

Androvicova, R., Horacek, J., Stark, T., Drago, F., Micale V. (2017). Endocannabinoid system in sexual motivational processes: Is it a novel therapeutic horizon?. Pharmacol Res, 115, 200-208. https://doi.org/10.1016/j.phrs.2016.11.021 PMID: 27884725

Breivogel, C.S., McPartland, J.M., Parekh B. (2018). Investigation of non-CB1, non-CB2 WIN 55212-2-sensitive G-protein-coupled receptors in the brains of mammals, birds, and amphibians. J Recept Signal Transduct Res, 38(4),316-326. https://doi.org/10.1080/10799893.2018.1494743 PMID: 30376752

Cardona Cano, S., Merkestein, M., Skibicka, K.P., Dickson, S.L., Adan, R.A. (2012). Role of ghrelin in the pathophysiology of eating disorders: implications for pharmacotherapy. CNS Drugs, 26, 281-296. https://doi.org/10.2165/11599890-000000000-00000 PMID: 22452525

D'Addario, C., Micioni Di Bonaventura, M.V., Pucci, M., Romano, A., Gaetani, S., Ciccocioppo, R., Cifani, C., Maccarrone, M. (2014). Endocannabinoid signaling and food addiction. Neurosci Biobehav Rev, 47, 203-224. https://doi.org/10.1016/j.neubiorev.2014.08.008 PMID: 25173635

Date, Y., Shimbara, T., Koda, S., Toshinai, K., Ida, T., Murakami, N., Miyazato, M., Kokame, K., Ishizuka, Y., Ishida, Y., Kageyama, H., Shioda, S., Kangawa, K., Nakazato, M. (2006). Peripheral ghrelin transmits orexigenic signals through the noradrenergic pathway from the hindbrain to the hypothalamus. Cell Metabol, 4, 323-331. https://doi.org/10.1016/j.cmet.2006.09.004 PMID: 17011505

Davis, J.L., Masuoka, D.T., Gerbrandt, L.K., Cherkin, A. (1979). Autoradiographic distribution of L-proline in chicks after intracerebral injection. Physiol Behav, 22, 693-695. PMID: 482410

Emadi, L., Jonaidi, H., Hosseini Amir Abad, E. (2011). The role of central CB2 cannabinoid receptors on food intake in neonatal chicks. J Comp Physiol A, 197,1143–1147. https://doi.org/10.1007/s00359-011-0676-z PMID: 21927979

Engel, J.A., Nylander, I., Jerlhag, E. (2015). A ghrelin receptor (GHS-R1A) antagonist attenuates the rewarding properties of morphine and increases opioid peptide levels in reward areas in mice. Eur Neuropsychopharmacol, 25, 2364–2371. https://doi.org/10.1016/j.euroneuro.2015.10.004 PMID: 26508707

Fuente-Martín, E., García-Cáceres, C., Argente-Arizón, P., Díaz, F., Granado, M., Freire-Regatillo, A., Castro-González, D., Ceballos, M.L., Frago, L.M., Dickson, S.L., Argente, J., Chowena, J.A. (2016). Ghrelin regulates glucose and glutamate transporters in hypothalamic astrocytes. Neuropharmacology, 73, 274-283. https://doi.org/10.1038/srep23673 PMID: 27026049

Furuse, M., Ando, R., Bungo, T., Ao, R., ShimoJO, M., Masuda, Y. (1999). Intracerebroventricular injection of orexins does not stimulate food intake in neonatal chicks. Br Poult Sci, 40, 698-700. https://doi.org/10.1080/00071669987115 PMID: 10670685

Furuse, M., Matsumoto, M., Saito, N., Sugahara, K., Hasegawa, S. (1997). The central corticotropin-releasing factor and glucagon-like peptide-1 in food intake of the neonatal chick. Eur J Pharmacol, 339, 211-214. PMID: 9473137

Hassanpour, S., Zendehdel, M., Babapour, V., Charkhkar, S. (2015). Endocannabinoid and nitric oxide interaction mediates food intake in neonatal chicken. Br Poult Sci, 56(4), 443-451. https://doi.org/10.1080/00071668.2015.

1059407 PMID: 26053311

Ierucka-Rybak, M., Wolak, M., Juszczak, M., Drobnik, J., Bojanowska E. (2016). The inhibitory effect of combination treatment with leptin and cannabinoid cb1 receptor agonist on food intake and body weight gain is mediated by serotonin 1B and 2C receptors. J Physiol Pharmacol, 67(3), 457-463. PMID: 27512006

Kaiya, H., Kangawa, K., Miyazato, M. (2013). What is the general action of ghrelin for vertebrates? - comparisons of ghrelin's effects across vertebrates. Gen Comp Endocrinol, 181,187-91. https://doi.org/10.1016/j.ygcen.2012.10.015 PMID: 23178701

Kaiya, H., Miyazato, M., Kangawa, K. (2011). Recent advances in the phylogenetic study of ghrelin. Peptides, 32, 2155-2174. https://doi.org/10.1016/j.peptides.2011.04.027 PMID: 21600258

Kalafateli, A.L., Vallöf, D., Jörnulf, J.W., Heilig, M., Jerlhag, E. (2018). A cannabinoid receptor antagonist attenuates ghrelin-induced activation of the mesolimbic dopamine system in mice. Physiol Behav, 184, 211–219. https://doi.org/10.1016/j.physbeh.2017.12.005 PMID: 29221808

Kitazawa, T., Teraoka, H., Kaiya, H. (2017). The chicken is an interesting animal for study of the functional role of ghrelin in the gastrointestinal tract. Endocr J, 64(Suppl.),S5-S9. https://doi.org/10.1507/endocrj.64.S5 PMID: 28652545

Lim, C.T., Kola, B., Feltrin, D., Perez-Tilve, D., Tschöp, M.H., Grossman, A.B., Korbonits, M. (2013). Ghrelin and cannabinoids require the ghrelin receptor to affect cellular energy metabolism. Mol Cell Endocrinol, 365, 303–308. https://doi.org/10.1016/j.mce.2012.11.007 PMID: 23178796

Müller, T.D.R. Nogueiras, M.L., Andermann, Z.B., Andrews, S.D., Anker, J., Argente, R.L., Batterham, S.C., Benoit, C.Y., Bowers, F., Broglio, F.F., et al. (2015). Ghrelin. Molecular Metabolism, 4(6), 437-460. https://doi.org/10.1016/j.molmet.2015.03.005 PMID: 26042199

Novoseletsky, N., Nussinovitch, A., Friedman-Einat, M. (2011). Attenuation of food intake in chicks by an inverse agonist of cannabinoid receptor 1 administered by either injection or ingestion in hydrocolloid carriers. Gen Comp Endocrinol, 170, 522-527. https://doi.org/10.1016/j.ygcen.2010.11.011 PMID: 21094647

Olanrewaju, H.A., Purswell, J., Collier, S.D., Branton, S.L. (2017). Effects of light ingress through ventilation fan apertures on selected blood variables of male broilers. Int J poult Sci, 16, 288-295.

Pingwen, Xu., Siegel, P.B., Denbow, D.M. (2011). Genetic selection for body weight in chickens has altered responses of the brain's AMPK system to food intake regulation effect of ghrelin, but not obestatin. Behav Brain Res, 221, 216-226. https://doi.org/10.1016/j.bbr.2011.02.034 PMID: 21376757

Qi, W., Ding, D., Salvi, R.J. (2008). Cytotoxic effects of dimethyl sulphoxide (DMSO) on cochlear organotypic cultures. Hear Res, 236, 52-60. https://doi.org/10.1016/j.heares.2007.12.002 PMID: 18207679

Saito, E.S., Kaiya, H., Tachibana, T., Tomonaga, S., Denbow, D.M., Kangawa, K., Furuse, M. (2005). Inhibitory effect of ghrelin on food intake is mediated by the corticotropin-releasing factor system in neonatal chicks. Regul Pept, 125, 201-208. https://doi.org/10.1016/j.regpep.2004.09.003 PMID: 15582733

Senin, L.L., Al-Massadi, O., Folgueira, C., Castelao, C., Pardo, M., et al. (2013). The Gastric CB1 receptor modulates ghrelin production through the mtor pathway to regulate food intake. PLoS ONE, 8(11), e80339. https://

doi.org/10.1371/journal.pone.0080339

Skibicka, K.P., Shirazi, R.H., Hansson, C., Dickson, S.L. (2012). Ghrelin interacts with neuropeptide Y Y1 and opioid receptors to increase food reward. Endocrinology, 153,1194-1205. https://doi.org/10.1507/endocrj.64.S5 PMID: 28652545

Skibicka, K.P., Shirazi, R.H., Rabasa-Papio, C., Alvarez-Crespo, M., Neuber, C., Vogel, H., Dickson, S.L. (2013). Divergent circuitry underlying food reward and intake effects of ghrelin: Dopaminergic VTA-accumbens projection mediates ghrelin's effect on food reward but not food intake. Neuropharmacology, 73, 274-283. https://doi.org/10.1016/j.neuropharm.2013.06.004 PMID: 23770258

Van Tienhoven, A., Juhasz, L.P. (1962). The chicken telencephalon, diencephalon and mesencephalon in sterotaxic coordinates. J Comp Neurol, 118,185-197. https://doi.org/10.1002/cne.901180205

Wiley, J.L., Marusich, J.A., Zhang, Y., Fulp, A., Maitra, R., Thomas, B.F., Mahadevan, A. (2012). Structural analogs of pyrazole and sulfonamide cannabinoids: effects on acute food intake in mice. Eur J Pharmacol, 695,62-70. https://doi.org/10.1016/j.ejphar.2012.08.019 PMID: 22975289

Zendehdel, M., Hassanpour, S. (2014). Ghrelin-induced hypophagia is mediated by the β2 adrenergic receptor in chicken. J Physiol Sci, 64, 383-391. https://doi.org/10.1007/s12576-014-0330-y PMID: 25080314

Zendehdel, M., Mokhtarpouriani, K., Hamidi, F., Montazeri, R. (2012). Intracerebroventricular injection of ghrelin produces hypophagia through central serotonergic mechanisms in chicken. Vet Res Commun, 37(1), 37-41. https://doi.org/10.1007/s11259-012-9544-8 PMID: 23065457

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نقش سیستم کانابینویدرژیک مرکزی بر هیپوفاژی ناشی از گرلین در جوجه‌های نژاد تخمگذار

محمدرضا طاهریان[۱]، مرتضی زنده‌دل[۲]، شاهین حسن‌پور[۳]

[۱]دانشکده کشاورزی، گروه علوم دامی، واحد کاشمر، دانشگاه آزاد اسلامی، کاشمر، ایران
[۲]گروه علوم پایه، دانشکده دامپزشکی، دانشگاه تهران، تهران، ایران
[۳]گروه علوم پایه، دانشکده دامپزشکی، واحد علوم و تحقیقات، دانشگاه آزاد اسلامی، تهران، ایران

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چکیده

زمینه مطالعه: رفتار تغذیه‌ای از طریق مسیرهای پیچیده‌ای تنظیم می‌شود که بواسطه سیگنال‌های سیستم عصبی مرکزی و محیطی انجام می‌شود.

هدف: هدف مطالعه حاضر، بررسی نقش سیستم کانابینویدرژیک مرکزی بر هیپوفاژی ناشی از گرلین در جوجه‌های نژاد تخمگذار ۳ ساعت محروم از غذا بود.

روش کار: در آزمایش ۱، جوجه‌های ۵ روزه تزریق داخل بطنی مغزی محلول کنترل، گرلین (۰/۶ نانومول)، SR۱۴۱۷۱۶A (آنتاگونیست انتخابی گیرنده‌های CB۱ کانابینوئیدی، ۶/۲۵ میکروگرم) و گرلین + SR۱۴۱۷۱۶A را دریافت کردند. در آزمایش دوم، جوجه‌ها تزریق داخل بطنی مغزی محلول کنترل، گرلین (۰/۶ نانومول)، AM۶۳۰ (آنتاگونیست انتخابی گیرنده‌های CB۲ ، ۱/۲۵ میکروگرم) و گرلین + AM۶۳۰را دریافت کردند. در آزمایش سوم، جوجه‌ها تزریق داخل بطنی مغزی محلول کنترل،۲-AG (آگونیست انتخابی گیرنده‌های CB۱ ، ۲ میکروگرم)، GSK۱۶۱۴۳۴۳ (آنتاگونیست گیرندهای گرلین، ۲ نانومول) و ۲-AG + GSK۱۶۱۴۳۴۳ را دریافت کردند. در آزمایش چهارم، جوجه‌ها تزریق داخل بطنی مغزی محلول کنترل، CB۶۵ (آگونیست انتخابی گیرنده‌های CB۲، ۶/۲۵ میکروگرم)، GSK۱۶۱۴۳۴۳ (آنتاگونیست گیرندهای گرلین، ۲ نانومول) وCB۶۵ + GSK۱۶۱۴۳۴۳ را دریافت کردند. سپس مصرف تجمعی خوراک تا ۱۲۰ دقیقه پس از تزریق اندازه‌گیری شد.

نتایج: باتوجه به نتایج بدست آمده، تزریق گرلین بطور معنی‌داری موجب کاهش مصرف تجمعی خوراک شد($P<۰/۰۵$). تزریق توام گرلین + SR۱۴۱۷۱۶A بطور معنی‌داری موجب تقویت هیپوفاژی ناشی از گرلین در مقایسه با گروه کنترل شد($P<۰/۰۵$). تزریق توام گرلین + AM۶۳۰ بطور معنی‌داری موجب تقویت هیپوفاژی ناشی از گرلین در مقایسه با گروه کنترل شد($P<۰/۰۵$). تزریق داخل بطنی مغزی ۲-AG (۲ میکروگرم)، موجب بروز هیپوفاژی شد ($P<۰/۰۵$). تزریق توام ۲-AG + GSK۱۶۱۴۳۴۳ و یا CB۶۵ + GSK۱۶۱۴۳۴۳ موجب افزایش مصرف غذا در مقایسه با گروه کنترل شد ($P<۰/۰۵$). همچنین، تزریق توام افزایش مصرف غذا در جوجه‌های محروم از غذا شد ($P<۰/۰۵$).

نتیجه گیری نهایی: نتایج نشان دهنده این بود که هیپوفاژی ناشی از گرلین از طریق گیرنده‌های CB۱ و CB۲ کانابینوئیدی در جوجه‌های نژاد تخمگذار وجود دارد.

واژه‌های کلیدی:
کانابینوئید، تنظیم مرکزی اخذ غذا، گرلین، جوجه‌های نژاد تخمگذار

نویسنده مسؤول: تلفن: ۴۴۸۶۸۵۶۰ (۲۱)۹۸+ نمابر: ۴۴۸۶۵۱۷۹ (۲۱)۹۸+ Email: hassanpour.shahin@gmail.com