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Central serotoninergic system mediates Neuromedin S (NMS) induced hypophagia in layer-type chicken

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A B S T R A C T

According to previous studies, the serotonergic system plays a remarkable role in regulating meal intake, however, its role in the mediation of feeding caused by neuromedin S (NMS) has not been investigated in birds. In the present research, 5 trials were considered in order to determine the links between these systems. In treatment 1, chickens received intracerebroventricular (ICV) infusion of NMS (0.25, 0.5, and 1 nmol). NMS (1 nmol), SB242084 (1.5 µg), a 5-HT2C receptor antagonist, and NMS + SB242084 were injected in the treatment 2. In subsequent treatments, instead of SB242084, 8-OH-DPAT (agonist of 5-HT1A receptor, 15.25 nmol), PCPA (serotonin synthesis inhibitor, 1.25 µg), and Fluoxetine (serotonin reuptake inhibitor, 10 µg) were applied. Then, total food consumption was recorded for 120 minutes. Based on observations, NMS dose-dependently attenuated meal intake ($P<0.05$). Hypophagia was diminished with NMS + SB242084 administration ($P<0.05$). ICV infusion of NMS + 8-OH-DPAT had no significant effect on the hypophagia ($P\geq0.05$). The NMS-induced decreasing feed intake was attenuated with co-infusion of NMS+ PCPA ($P< 0.05$). Also, hypophagia was strengthened by NMS+ Fluoxetine co-infusion ($P< 0.05$). According to the results, the NMS-induced hypophagia is possibly mediated via 5-HT2c receptors in layer-type chickens.

Keywords: *Neuromedin S; Serotonergic receptors; Food intake; Layers; Hypophagia*

1 Introduction

The brain integrates messages received from the digestive tract and other peripheral organs with signals produced in different brain areas to regulate food intake. Among different brain regions, hypothalamus nuclei play the most important role in gathering and processing nutritional messages (1). Also, the interaction between

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different neurotransmitters has notable effects on the formation of complex physiological mechanisms related to feeding behaviors (2). To date, various neurotransmitters have been identified in birds and mammals, and their number is still increasing (3). In addition to investigating the independent role of each of the neurotransmitters on appetite, researchers also investigate their interaction with other regulatory systems involved. Considering the observed differences in the function of some of these factors between birds and mammals (3), it seems necessary to investigate the role of each of the neurotransmitters in regulating the appetite of birds.

Neuromedin S (NMS) was first isolated from rat brains in 2005 and identified as an anorectic peptide in mammals in 2008 (4). Based on experiments conducted on the central effects of this peptide on feed intake in mammals, it was found that NMS has a high affinity for binding to the Neuromedin U (NMU) receptor-2. After intracerebroventricular (ICV) injection, NMS has inhibitory effects on food intake by binding to this receptor (5). Deletion of this receptor in the mouse brain appears to abolish the food intake effects after ICV injection of NMS (6). Based on a study on birds by Tachibana et al. (2014), ICV injection of NMS at a dose of 1 nmol was shown to induce hypophagic effects in food-deprived laying hens as well as in birds with free access to food and water, such as mammals (7). The relationship between glucose level and fat metabolism with NMS was also proven in egg-type chickens. Research findings show that central administration of NMS in chickens increases chicken activity but does not increase food consumption behavior (8). Although the existence of the NMU-2 receptor has been established in birds, more experiments are needed to understand the mechanism of NMS efficacy through this receptor (9).

Serotonin (5-HT) is a monoamine neurotransmitter which function has been investigated in the control of feeding behavior (10). Among the examined serotonin receptors, 5HT2C and 5HT1B have been used in most joint researches and their role in regulating appetite and food intake has been well demonstrated (11, 12). Based on the studies, it seems that the stimulation of some serotonin receptors causes a decrease in food consumption and some other causes an increase in meal consumption in birds and mammals. In this regard, in research following the injection of 5HT1A agonist in 10-week-old male chickens 15 minutes before feeding, a decrease in food consumption was observed, while there was no effect on water intake (13). Also, injecting this drug one hour after feeding stimulated meal intake, but it had no effect on water drinking (13). However, according to another study, ICV and intraperitoneal (IP) administration of 5HT2C agonist in quail resulted in hypophagic effects of this neurotransmitter, and ICV injection of its antagonist inhibited hypophagia (14). In general, most studies show that stimulation of the central serotonergic system reduces the intake of food and water in birds.

Undoubtedly, there are genetic and physiological differences between broiler and layer chickens based on their production goals. Broiler chickens are bred for rapid muscle production and weight gain in a short period of time, and laying chickens are bred for high efficiency in egg production. Therefore, by conducting independent studies on each of these types, unique information can be obtained. There is little information about the interaction of NMS with the serotonergic system in controlling the activities of the central nervous system (CNS). According to the authors' search, so far, no study has investigated the interaction between the serotonergic system and NMS in regulating the feeding behavior of birds. Therefore, the current research was conducted with the aim of evaluating the mediation role of the serotonergic system in meal consumption caused by NMS in egg-type chickens.

2 Methods and Materials

2.1 Animals

A total of 220 one-day-old layer chickens were procured (from Morghak Company near Tehran, Iran). Chicks were kept in common cages for two days, then they were placed in individual cages for three days. Drinking water and a commercial starter diet were available to the birds during all phases of the study. The conditions of the chickens' keeping environment were kept constant in terms of humidity (40–50%), temperature (32 °C ± 1), and lighting (23:1 lighting/dark period) (15). Finally, the chickens were injected when they were five days old. Three hours before the injection, while the chickens had free access to water, they were deprived of food. All experimental procedures were performed according to US guidelines (Publication No. 23-85, revised 1996) and approved by the Institutional Animal Ethics Committee of the Faculty of Veterinary Medicine, University of Tehran.

2.2 Drugs

Drugs consisted of NMS, SB242084 (antagonist of 5-HT2C receptor), 8-OH-DPAT (agonist of 5-HT1A

receptor), PCPA (Serotonin synthesis inhibitor), Fluoxetine (serotonin reuptake inhibitor), and Evans Blue (Sigma, USA). All the mentioned compounds were prepared in a solution of dimethyl sulfoxide (DMSO) which was diluted with 0.85% NaCl 0.9% plus dye at a ratio of 1:250. The dye mixture containing DMSO + Saline was used as a control solution in all treatment groups. It should be noted that DMSO did not have cytotoxic effects in the dose used in this study (16).

2.3 ICV Infusion

Before the experiments, the layers were divided into different trial groups based on their weight, so that the average body weight in different groups was almost the same. In this research, a total of 20 experimental groups were used in 5 experiments (the number of chickens in each experimental group = 12). In each chicken, ICV infusion was done using a microsyringe (Hamilton, Switzerland) without surgery and anesthesia (17, 18). Using an acrylic device, the head of the bird was placed parallel to the surface of the table (19). Then a hole was created in the right lateral ventricle of the brain. During the injection, the tip of the needle penetrated 4 mm into the skull. All solutions were injected in a volume of 10 µl. It should be noted that this method did not cause any physiological stress in the birds (20). Finally, layers were ethically euthanized (according to the AVMA Guidelines for Animal Euthanasia "No.: M3.6, Cervical Dislocation)" and the injection sites were checked for the presence of color and to confirm the correctness of the injection.

2.4 Food Consumption Measurement

The treatment groups are shown in Table 1. The prescribed doses of drugs were based on previous research (21, 22). After ICV infusion, the layers were returned to the individual boxes while water and pre-weighed food were provided. Cumulative feed consumption was recorded at 30, 60, and 120 minutes after administration. In order to eliminate or minimize the effect of chicken weight on meal intake, cumulative meal intake was calculated as a body weight percentage (%BW).

Table 1. ICV injections in experiments

Groups	Exp.1	Exp.2	Exp.3	Exp.4	Exp.5
A	Control solution	Control solution	Control solution	Control solution	Control solution
B	NMS (0.25 nmol)	SB242084 (5-HT2c receptor antagonist) (1.5 µg)	8-OH-DPAT (5-HT1A receptor agonist) (15.25 nmol)	PCPA (serotonin synthesis inhibitor) (1.25 µg)	Fluoxetine (serotonin reuptake inhibitor) (10 µg)
C	NMS (0.5 nmol)	NMS (1 nmol)	NMS (1 nmol)	NMS (1 nmol)	NMS (1 nmol)
D	NMS (1 nmol)	SB242084+ NMS (1.5 µg)+ (1 nmol)	8-OH-DPAT+ NMS (15.25 nmol)+ (1 nmol)	PCPA+ NMS (1.25 µg)+ (1 nmol)	Fluoxetine+ NMS (10 µg)+ (1 nmol)

2.5 Statistical Analysis

The results of the experiments were presented as mean ± SEM. Total feed consumption (as %BW) was analyzed by repeated measure two-way analysis of variance (ANOVA) and means compared by the Tukey-Kramer test. $P<0.05$ was considered meaningful differences among groups.

3 Results

In treatment 1, the ICV infusion of 0.25 nmol NMS had no remarkable effect on meal consumption ($P\geq0.05$), while the infusion of 0.5 and 1 nmol of NMS dose-dependently and significantly attenuated the meal intake ($P<0.05$) (Figure 1).

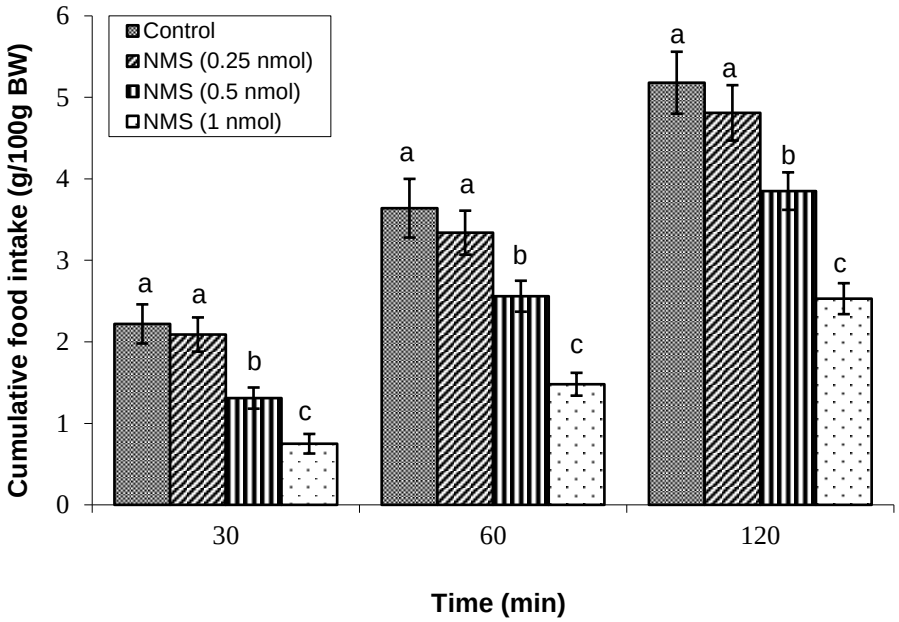

Figure 1. Effects of intracerebroventricular infusion of control solution and NMS (0.25, 0.5 and 1 nmol) on cumulative food consumption in neonatal layers (n=44). Data are expressed as mean ± SEM. Different letters (a, b and c) indicate significant differences between groups (P<0.05).

Regarding treatment 2, SB242084 administration alone did not affect meal consumption (P≥ 0.05). In addition, the NMS-induced hypophagia was notably decreased via co-infusion of NMS + SB242084 (P<0.05) (Figure 2).

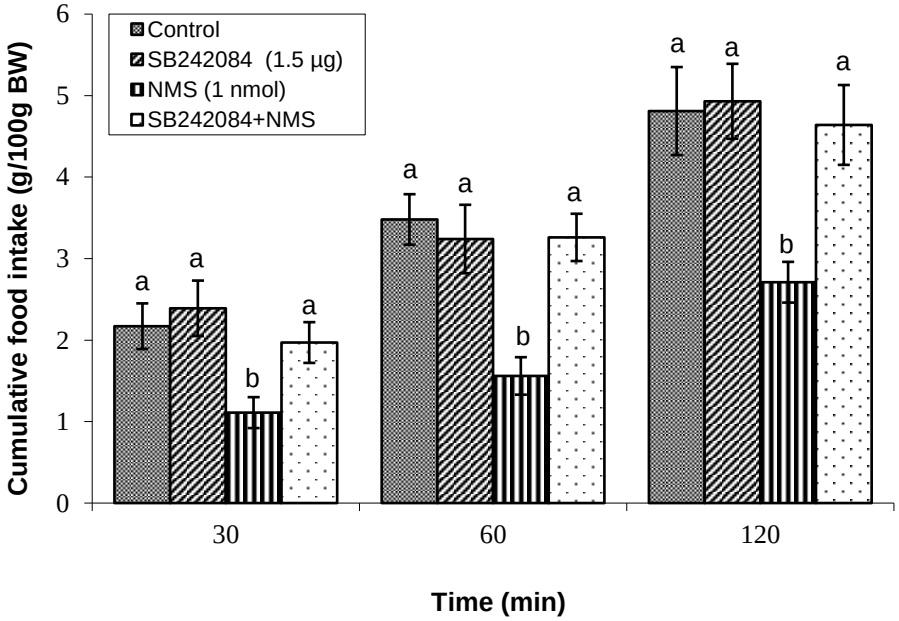

Figure 2. Effects of intracerebroventricular infusion of control solution, SB242084 (1.5 µg), NMS (1 nmol), and NMS + SB242084 on cumulative food consumption in neonatal layers (n=44). SB242084: 5-HT2c receptor antagonist. Data are expressed as mean ± SEM. Different letters (a, and b) indicate significant differences between groups (P<0.05).

In the third treatment, an infusion of 15.25 nmol 8-OH-DPAT made no significant change in meal intake (P≥0.05). The NMS-induced hypophagia was not altered via co-administration of NMS + 8-OH-DPAT at all times (P≥ 0.05) (Figure 3).

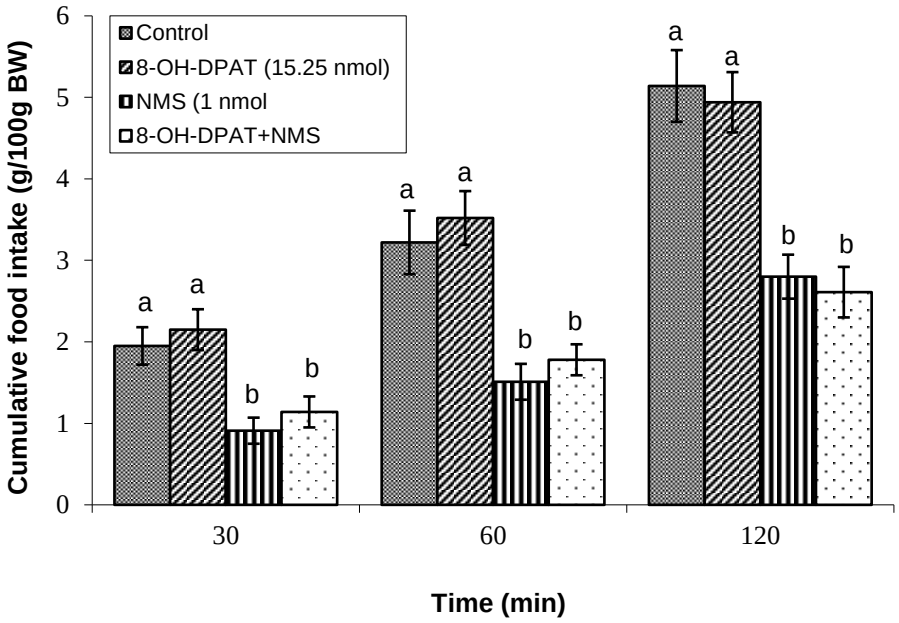

Figure 3. Effects of intracerebroventricular infusion of control solution, 8-OH-DPAT (15.25 nmol), NMS (1 nmol), and NMS + 8-OH-DPAT on cumulative food consumption in neonatal layers (n=44). 8-OH-DPAT: 5-HT1A receptor agonist. Data are expressed as mean ± SEM. Different letters (a, and b) indicate significant differences between groups (P<0.05).

In treatment 4, ICV infusion of 1.25 µg PCPA didn't change cumulative food consumption noticeably (P≥0.05). The hypophagic effect of NMS was remarkably attenuated via the administration of NMS + PCPA rather than the control treatment (P<0.05) (Figure 4).

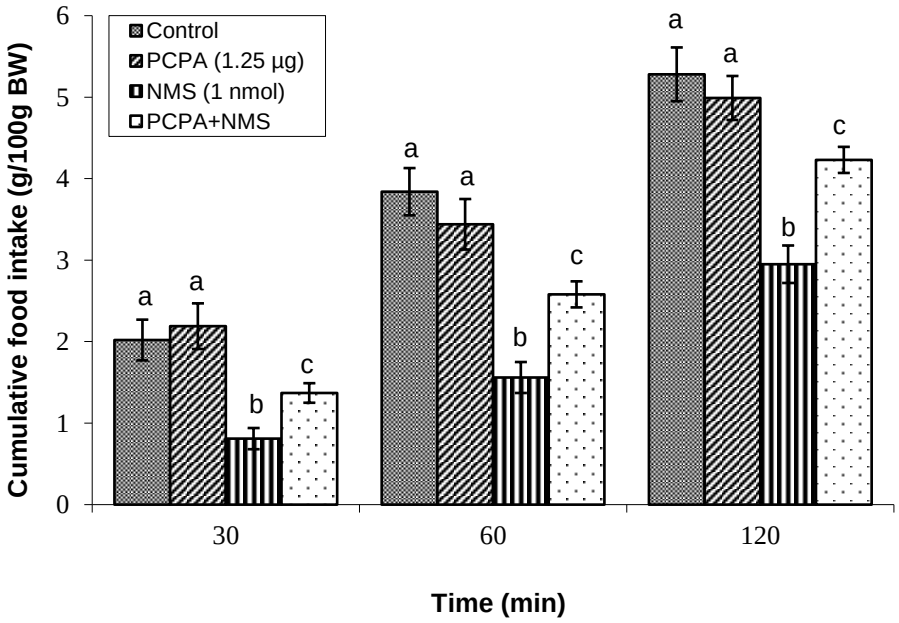

Figure 4. Effects of intracerebroventricular infusion of control solution, PCPA (1.25 µg), NMS (1 nmol), and NMS + PCPA on cumulative food consumption in neonatal layers (n=44). PCPA: serotonin synthesis inhibitor. Data are expressed as mean ± SEM. Different letters (a, b, and c) indicate significant differences between groups (P<0.05).

In the fifth treatment, the administration of Fluoxetine (10 µg) alone had no impact on the feeding of chickens (P≥0.05). The NMS-induced hypophagia was remarkably amplified via infusion of NMS + Fluoxetine at all times after ICV injection (P<0.05) (Figure 5).

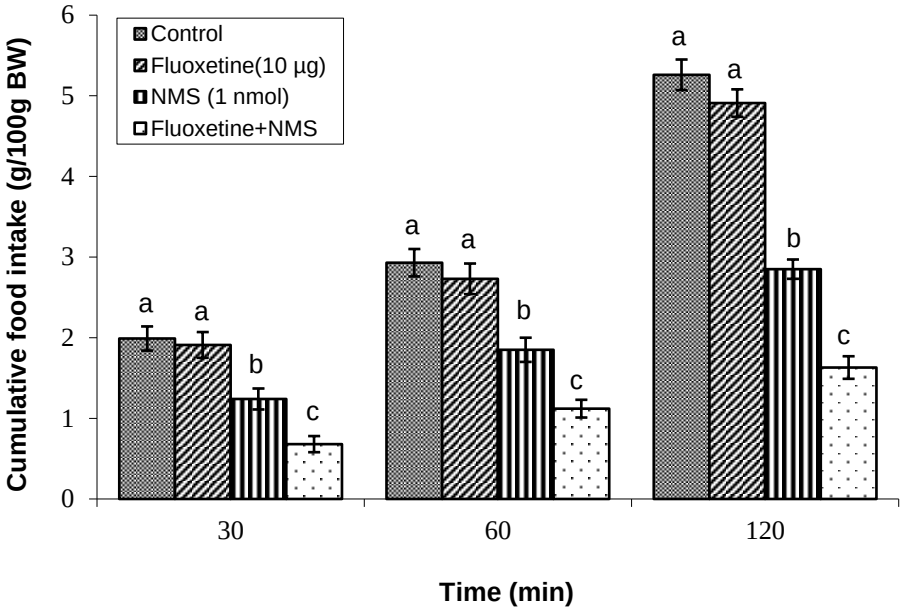

Figure 5. Effects of intracerebroventricular infusion of control solution, Fluoxetine (10 µg), NMS (1 nmol), and NMS + Fluoxetine on cumulative food consumption in neonatal layers (n=44). Fluoxetine: serotonin reuptake inhibitor. Data are expressed as mean ± SEM. Different letters (a, b, and c) indicate significant differences between groups (P<0.05).

4 Discussion

During the last few decades, many advances have been made regarding the identification of factors affecting the regulation of feed consumption, and along with the introduction and recognition of the function of these factors, investigating their interactions has become more important. According to the data obtained from the present study, the ICV infusion of NMS (0.25 nmol) had no meaningful effect on the amount of meal consumed by chickens, while its administration in doses of 0.5 and 1 nmol significantly reduced meal intake in layers. Based on the experiments, NMS (including 36 amino acids) has a common C-terminal core structure (residues of seven amino acids) with NMU and activates NMU1 and NMU2 receptors (23). However, NMS cannot be considered a linked type of NMU because genetic mapping has shown the discrete chromosomes of these two neuropeptides. On the other hand, differences in their mRNA presence areas have also been observed, so that NMS was distributed in the testis, spleen, and, brain, while NMU mRNAs were detected in different organs (24). NMU has been proposed as an anorectic neuropeptide that exerts its effect mainly through NMUR2 in the paraventricular nucleus (PVN) (25). A number of studies have shown that central administration of NMU in chickens and rodents reduces food intake (26, 27). In another study, hyperphagic effect caused by central injection of NMU antagonist was reported in mice (28). In addition, it has been documented that IP infusion of NMU reduces feeding in rodents (29). In the study of Ghashghayi et al. (2022) on neonatal chickens, ICV injection of NMU caused a dose-dependent decrease in food consumption. Also, based on the findings of their experiments, the hypophagic effect of NMU was mediated via serotonergic, dopaminergic, and GABAergic systems (30). Considering the structural similarity between NMU and NMS and the effect of NMS on NMU receptors, it is possible to compare the effects of these two neuropeptides on the feed consumption of birds. Therefore, the appetite-reducing effect caused by the central administration of NMS in the present study can be considered in line with NMU-induced hypophagia. Regarding NMS, in a study conducted on rats in 2012, the high expression of this peptide was proven in the suprachiasmatic nucleus (SCN), PVN, and the arcuate nucleus (ARC) of the hypothalamus (31). The mentioned areas play a significant role in regulating different physiological functions of the body, especially feeding

behavior (32). In a study on rats, the hypophagic effect of NMS following the ICV administration was observed up to 12 hours after the injection in the dark period. Also, the mediation of melanocortinergic and corticotropinergic systems was observed in the occurrence of this effect (33). In laying chickens, the study of Gholami Ahmedabadi et al. (2022) showed hypophagia induced by central administration of NMS. In addition, it was found that this appetite-reducing effect is mediated via dopaminergic and adrenergic receptors (22). The mentioned results are similar to the observations of the current research, indicating the reducing effect of NMS on meal consumption.

Studies on the effects of the serotonergic system on feeding behavior regulation have shown that the hypophagic effects caused by 5-HT ICV injection can be mediated via 5-HT1A and 5-HT2C receptors (11). It is worth noting that central infusion of 5-HT1A agonist (8-OH-DPAT) in birds with 24 hours of food deprivation increased the time interval of food intake, while it had no significant effect on the amount of meal consumed (34). Furthermore, central administration of serotonin was able to reduce food intake in free-access or food-deprived pigeons, turkeys, and chickens (35). In another study, it was observed that central administration of 5-HT resulted in the attenuation of feeding in meat-type chickens with free access to food. However, it had no meaningful effect on meal consumption of food-deprived chickens (36). In this study, we demonstrated that the inhibitory effect of NMS on meal consumption was significantly attenuated via PCPA (serotonin synthesis inhibitor) ($P<0.05$), whereas this effect was enhanced by fluoxetine (5-HT reuptake inhibitor) pretreatment ($P<0.05$). Also, the reduction of food intake induced via central infusion of NMS was not remarkably altered by pretreatment with 8-OH-DPAT (agonist of 5-HT1A receptor) ($P\geq0.05$), but this effect was enhanced with co-infusion of SB242084 (antagonist of 5-HT2C receptor) ($P<0.05$).

Based on our search, there has been no previous study on the interaction effect between the central 5-HTergic system and NMS on food intake in birds, so it was not possible to compare the current observations with prior experiments. The findings of the present research indicate that the reduction in food intake caused by serotonin is probably done through 5-HT2C receptors in layer chicks. Finally, the authors recommend conducting more experiments based on identifying the molecular and cellular signaling pathways of these systems and their interaction with other neural mediators involved in the regulation of poultry appetite.

Conflict of Interest

The authors declared no conflicts of interest.

Author Contributions

MRP: writing- original draft preparation, SB contributed to review and editing, AM participated in the provision of data set, JR contributed to the conception of study and supervision. All authors read and approved the final manuscript.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

Ethical Considerations

All ethical principles were fully observed in this study in accordance with the guidelines of the Ethical Committee of the Faculty of Veterinary Medicine, University of Tehran. The research protocol was reviewed and approved under the ethical approval code IR.UT.VETMED.REC. 7508007-6-42/2022.

References

1. Roger C, Lasbleiz A, Guye M, Dutour A, Gaborit B, Ranjeva J-P. The role of the human hypothalamus in food intake networks: An MRI perspective. Frontiers in nutrition. 2022;8:760914. [PMID: 35047539] [PMCID: PMC8762294] [DOI]
2. Gasmi A, Nasreen A, Menzel A, Gasmi Benahmed A, Pivina L, Noor S, et al. Neurotransmitters Regulation and Food Intake: The Role of Dietary Sources in Neurotransmission. Molecules. 2022;28(1):210. [PMID: 36615404] [PMCID: PMC9822089] [DOI]
3. Shojaei M, Yousefi AR, Zendehdel M, Khodadadi M. Food Intake Regulation in Birds: the Role of Neurotransmitters and Hormones. Iranian Journal of Veterinary Medicine. 2020;14(1).
4. Mori K, Miyazato M, Ida T, Murakami N, Serino R, Ueta Y, et al. Identification of neuromedin S and its possible role in the mammalian circadian oscillator system. The EMBO journal. 2005;24(2):325-35. [PMID: 15635449] [PMCID: PMC545815] [DOI]
5. Peier A, Kosinski J, Cox-York K, Qian Y, Desai K, Feng Y, et al. The antiobesity effects of centrally administered neuromedin U and neuromedin S are mediated predominantly by the neuromedin U receptor 2 (NMUR2). Endocrinology. 2009;150(7):3101-9. [PMID: 19324999] [PMCID: PMC2703546] [DOI]
6. Yokogi K, Goto Y, Otsuka M, Ojima F, Kobayashi T, Tsuchiba Y, et al. Neuromedin U-deficient rats do not lose body weight or food intake. Scientific reports. 2022;12(1):17472. [PMID: 36302800] [PMCID: PMC9614009] [DOI]
7. Tachibana T, Matsuda K, Khan MSI, Ueda H, Cline MA. Feeding and drinking response following central administration of neuromedin S in chicks. Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology. 2010;157(1):63-7. [PMID: 20451649] [DOI]
8. Peier AM, Desai K, Hubert J, Du X, Yang L, Qian Y, et al. Effects of peripherally administered neuromedin U on energy and glucose homeostasis. Endocrinology. 2011;152(7):2644-54. [PMID: 21586559] [DOI]

9. Wan Y, Zhang J, Fang C, Chen J, Li J, Li J, et al. Characterization of neuromedin U (NMU), neuromedin S (NMS) and their receptors (NMUR1, NMUR2) in chickens. Peptides. 2018;101:69-81. [PMID: 29288685] [DOI]
10. van Galen KA, Ter Horst KW, Serlie MJ. Serotonin, food intake, and obesity. Obesity Reviews. 2021;22(7):e13210. [PMID: 33559362] [PMCID: PMC8243944] [DOI]
11. Yousefi A, Shojaei M, Zendehdel M. Evaluation the role of central serotonin and 5HT2c serotonin receptor on feed intake in female layer-type Bovans chicken by intracerebroventricular (ICV) injection of Para-chlorophenylalanine and SB242084. Veterinary Research & Biological Products. 2019;32(1):55-62.
12. Rahmani B, Mahdavi K, Zendedel Kheybari M, Khodadadi M, Keshavarz M, Shahabi M, Baghbanzadeh A. Role of central opioid receptors on serotonin-Induced hypophagia in the neonatal broilers. Iranian Journal of Veterinary Science and Technology. 2022;14(1):9-19.
13. Saadoun A, Cabrera M. Effect of the 5-HT1A receptor agonist 8-OH-DPAT on food and water intake in chickens. Physiology & behavior. 2002;75(3):271-5. [PMID: 11897252] [DOI]
14. Cedraz-Mercez P, Almeida A, Castilhos L, Olivares E, Marinho Jr A, Medeiros M, Reis L. Influence of serotonergic transmission and postsynaptic 5-HT2C action on the feeding behavior of Coturnix japonica (Galliformes: Aves). Brazilian Journal of Biology. 2005;65:589-95. [PMID: 16532182] [DOI]
15. Olanrewaju H, Thaxton J, Dozier W, Purswell J, Roush W, Branton S. A review of lighting programs for broiler production. International journal of poultry science. 2006;5(4):301-8. [DOI]
16. Blevins JE, Stanley BG, Reidelberger RD. DMSO as a vehicle for central injections: tests with feeding elicited by norepinephrine injected into the paraventricular nucleus. Pharmacology Biochemistry and Behavior. 2002;71(1-2):277-82. [PMID: 11812533] [DOI]
17. Davis JL, Masuoka DT, Gerbrandt LK, Cherkin A. Autoradiographic distribution of L-proline in chicks after intracerebral injection. Physiology & Behavior. 1979;22(4):693-5. [PMID: 482410] [DOI]
18. Furuse M, Matsumoto M, Saito N, Sugahara K, Hasegawa S. The central corticotropin-releasing factor and glucagon-like peptide-1 in food intake of the neonatal chick. European journal of pharmacology. 1997;339(2-3):211-3. [PMID: 9473137] [DOI]
19. van Tienhoven At, Juhasz L. The chicken telencephalon, diencephalon and mesencephalon in stereotaxic coordinates. Journal of Comparative Neurology. 1962;118(2):185-97. [PMID: 13924637] [DOI]
20. Saito E-S, Kaiya H, Tachibana T, Tomonaga S, Denbow DM, Kangawa K, Furuse M. Inhibitory effect of ghrelin on food intake is mediated by the corticotropin-releasing factor system in neonatal chicks. Regulatory peptides. 2005;125(1-3):201-8. [PMID: 15582733] [DOI]
21. Zendehdel M, Mokhtarpouriani K, Babapour V, Baghbanzadeh A, Pourrahimi M, Hassanpour S. The effect of serotonergic system on nociceptin/orphanin FQ induced food intake in chicken. The Journal of Physiological Sciences. 2013;63(4):271-7. [PMID: 23615894] [DOI]
22. Ahmadabadi KG, Zendehdel M, Vazir B, Asghari A, Babapour V. Possible effects of the central adrenergic and dopaminergic receptors on hypophagia induced by neuromedin S in neonatal layer-type chicks. General and Comparative Endocrinology. 2022;321:114032. [PMID: 35331741] [DOI]
23. Raddatz R, Wilson AE, Artymyshyn R, Bonini JA, Borowsky B, Boteju LW, et al. Identification and characterization of two neuromedin U receptors differentially expressed in peripheral tissues and the central nervous system. Journal of Biological Chemistry. 2000;275(42):32452-9. [PMID: 10899166] [DOI]
24. Domin J, Ghatei MA, Chohan P, Bloom SR. Characterization of neuromedin U like immunoreactivity in rat, porcine guinea-pig and human tissue extracts using a specific radioimmunoassay. Biochemical and biophysical research communications. 1986;140(3):1127-34. [PMID: 3778484] [PMCID: PMC5554362] [DOI]
25. Graham E, Turnbull Y, Fotheringham P, Nilaweera K, Mercer J, Morgan PJ, Barrett P. Neuromedin U and neuromedin U receptor-2 expression in the mouse and rat hypothalamus: effects of nutritional status. Journal of neurochemistry. 2003;87(5):1165-73. [PMID: 14622096] [DOI]
26. Honda K, Saneyasu T, Okuda M, Uemura T, Kamisoyama H. Glucagon and neuromedin U suppress food intake in broiler chicks. The Journal of Poultry Science. 2015;52(4):268-73. [DOI]
27. Dalbøge LS, Pedersen SL, van Witteloostuijn SB, Rasmussen JE, Rigbolt KT, Jensen KJ, et al. Synthesis and evaluation of novel lipidated neuromedin U analogs with increased stability and effects on food intake. Journal of Peptide Science. 2015;21(2):85-94. [PMID: 25521062] [DOI]
28. Nakazato M, Hanada R, Murakami N, Date Y, Mondal MS, Kojima M, et al. Central effects of neuromedin U in the regulation of energy homeostasis. Biochemical and biophysical research communications. 2000;277(1):191-4. [PMID: 11027662] [DOI]
29. Kaisho T, Nagai H, Asakawa T, Suzuki N, Fujita H, Matsumiya K, et al. Effects of peripheral administration of a Neuromedin U receptor 2-selective agonist on food intake and body weight in obese mice. International Journal of Obesity. 2017;41(12):1790-7. [PMID: 28757640] [DOI]
30. Ghashghayi E, Zendehdel M, Khodadadi M, Rahmani B. Central dopaminergic, serotoninergic, as well as GABAergic systems mediate NMU-induced hypophagia in newborn chicken. International Journal of Neuroscience. 2022:1-11. [PMID: 35901030] [DOI]
31. Mori M, Mori K, Ida T, Sato T, Kojima M, Miyazato M, Kangawa K. Different distribution of neuromedin S and its mRNA in the rat brain: NMS peptide is present not only in the hypothalamus as the mRNA, but also in the brainstem. Frontiers in Endocrinology. 2012;3:152. [PMID: 23264767] [PMCID: PMC3524995] [DOI]
32. Anand BK, Brobeck JR. Localization of a "feeding center" in the hypothalamus of the rat. Proceedings of the society for experimental biology and Medicine. 1951;77(2):323-5. [PMID: 14854036] [DOI]
33. Ida T, Mori K, Miyazato M, Egi Y, Abe S, Nakahara K, et al. Neuromedin S is a novel anorexigenic hormone. Endocrinology. 2005;146(10):4217-23. [PMID: 15976061] [DOI]
34. Zendehdel M, Mokhtarpouriani K, Babapour V, Pourrahimi M, Hamidi F. The role of 5-HT2A and 5-HT2C receptors on harmalineinduced eating behavior in 24-h food-deprived broiler cockerels. Iranian Journal of Veterinary Research. 2013;14(2):94-9.
35. Baghaeikia S, Fallah H, Khodadadi M, Yousefvand S, Mahdavi K, Zendehdel M, Rahmani B. Opioid receptor μ, not δ and κ, modulate food intake induced by ghrelin in laying chickens. Canadian Journal of Physiology and Pharmacology. 2022;100(10):983-92. [PMID: 35819847] [DOI]

36. Sashihara K, Bungo T, Ando R, Ohgushi A, Kawakami S-I, Denbow D, Furuse M. Role of central serotonergic systems on the regulation of feeding behavior of chicks in two different strains. Journal of Applied Animal Research. 2002;21(1):17-23. [DOI]