

# The Effects of Dopamine and Glutamate Agonists on Brain Histology and Food Intake of Quails Exposed to Environmental Heat Stress

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## Abstract

The present study was aimed to investigate the effects of apomorphine (dopamine agonist) and glutamate on quails exposed to environmental heat stress. Thirty-two male Japanese quails were randomly divided into four groups. Control quails maintained at 25-27 °C temperature while heat stressed quails exposed to outdoor temperature ranging from 25 to 41.7 °C for four days. Heat stressed quails were received saline, apomorphine (2 mg/kg, intraperitoneal ly) or glutamate (2mg/kg, intraperitoneal ly). After two days food intake was recorded and then birds were euthanized to perform histopathological investigations. The cumulative food intake was significantly reduced in heat stressed quails, especially in the glutamate treated quails. The brain histopathological changes were even more severe in the heat-treated group. Treatment with apomorphine could reduce the adverse effects of heat stress on brain. These results showed the protective effects of apomorphine on heat stress-induced anorexia in quails.

**Keywords:** Quail, Heat stress disorders, Apomorphine, Glutamic acid

## Introduction

Heat stress is the main factor that could affect poultry industry all over the world, especially in the tropical region (1). The regulation of food intake is firmly related to the environmental factors and glutamate receptors (2). Heat stress is the main parameters that could affect food intake and weight gain in poultry industry (3). Previous studies have shown that heat stress could induce histological changes in different tissues including liver, heart and kidney (4). These impacts are mainly regulated through the interaction of several neuropeptides and neurotransmitters. Accumulating evidences have indicated that amino acids like glutamate and catecholamines such as epinephrine, norepinephrine and apomorphine, affect and control feeding behavior in birds and mammals exposed to heat stress (5, 6). Apomorphine - a non- selective dopamine agonist- have numerous physiological roles including food intake regulation birds (7). As shown in previous experiments, the administration of apomorphine increase appetite in rats and humans (8). It has been demonstrated that effect of neurotransmitters on water intake is evolutionarily conserved in quails, whereas its effect on food intake is in contrast to mammalian vertebrates (9). Intra-cerebroventricular (ICV) administration of dopamine in birds inhibits food intake. However, the effect of peripheral administration of dopamine agonists on food intake is not consistent with birds. Intravenous (IV) administration of dopamine decreases food intake in quails, whereas in adult Japanese quail, it increases food intake and weight gain (10). It has been reported that the effect of apomorphine on birds is in contrast to what has previously described in the experiments. It has also been reported that glutamate mediates the inhibitory effect of apomorphine in quails (11). The mechanism underlying the apomorphine - induced hypoplasia in birds is still unclear, although the Group 4: heat stressed quails received glutamate (2mg/kg, intraperitoneally) for four days. Glutamate (n= 8). Each bird

anorexic effect of beta receptors was reported to be mediated by serotonin but not histamine (12). The metabotropic and the inotropic glutamate receptor, was discovered in 1998. This neurotransmitter because of its unique effects, have diverse physiological roles in vertebrate including birds. It is also well-known fact that glutamate have an important role in controlling physiological responses to different environmental stresses including thermal changes and photoperiods (13). Intraperitoneal administration or systemic administration of glutamate and catecholamines could increase or decrease food intake in birds and mammals depending on environmental and physiological conditions (14-16).

Considering previous studies about the effects of apomorphine and glutamate on feeding Behavior, it can be hypothesized that both systems possibly affect appetite in response to changes in physiological and thermal conditions. To the best of our knowledge, there is no scientific reports regarding the effects of apomorphine and glutamate on food intake of quails under heat stress. Furthermore, recent work has suggested that acute or chronic heat stress could affect brain function or brain histology. Thus, the present study was carried out to examine the effects of apomorphine and glutamate administrations on food intake and brain histopathological changes of the brain in quails exposed to environmental heat stress.

## Materials and methods

Thirty-two adult male Japanese quails, weighing 90±5 gr was randomly divided into four groups. Group 1: control quails exposed to 25-27 °C temperature; Group 2: heat stressed quails exposed to outdoor temperature ranging from 25 to 41.7 °C for four days; Group 3: heat stressed quails received apomorphine (2 mg/kg, intraperitoneally) for four days; and was individually put in separate cages with free access to tap water and food. TI

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outdoor temperature on the two consecutive hot day in summer on June based on the meteorological reports. Effects of intraperitoneal feeding of apomorphine and glutamate on heat stress treated quails were determined. All solutions were injected on the same day during 09:00–12:00 in 8 birds per treatment, and the feeding behavior was monitored following the administrations. Birds were handled and mock-injected daily during the 5 days period to fed up with experimental procedure. Three hours before the experiments, birds were deprived of food but fresh water supplied ad lib. Immediately after administration s, the birds were returned to their cages, and feed intake (grams) was recorded at 120, and 240 min. The cumulative food intake by each bird was monitored throughout the experiments. After euthanasia, brain histopathology was performed. Doses of drugs were chosen on the basis of preliminary experiments and previous studies. Control group was treated with 2ml of % 0.9 Na Cl solution. Experimental handling and grouping treatments were conducted in-line to the Guidelines published by the US National Institute of Health (NIH publication No85-23, revised 1996) and also with the current laws of our university.

The cumulative pellet consumption of quails is presented as mean  $\pm$  SEM. The obtained food intake results were analyzed using a one-way analysis of variance (ANOVA) at each time interval. For treatment showing a main effect by ANOVA, means were compared by using the Tukey post hoc test. The

differences were considered significantly different when  $P \leq 0.05$ .

## Results

The feed intake response to intraperitoneal administration of apomorphine and glutamate in heat stressed quails is shown in Figures 1 to 4. In experiment 1, the exposure of quails to heat stress caused a decrease in food consumption (Figure 1,  $P \leq 0.05$ ). The apomorphine injection was unable to restore the food intake to normal levels however the food intake in apomorphine treated quails was higher in heat stress-treated quails. (Figure 1,  $P \leq 0.05$ ). As shown in Figure 1, glutamate completely increased the effect of heat stress on feed intake observed at 120- and 240-min post treatment. Histological investigation showed that brain of control quails had normal histological appearance with normal blood sinusoids and normal neurons (Figure 2) while the brain of heat stressed quails showed signs of brain damage including enlargement of blood sinusoids and neuronal degeneration (Figure 3). The histopathological investigation of quails exposed to heat stress and treated with dopamine showed signs of improvement such as a decrease in the size of blood sinusoids in brain and reduced neuronal necrosis (Figure 4). On the other hand, pretreatment with glutamate caused a prominent deterioration of brain histological appearance (Figure 5).

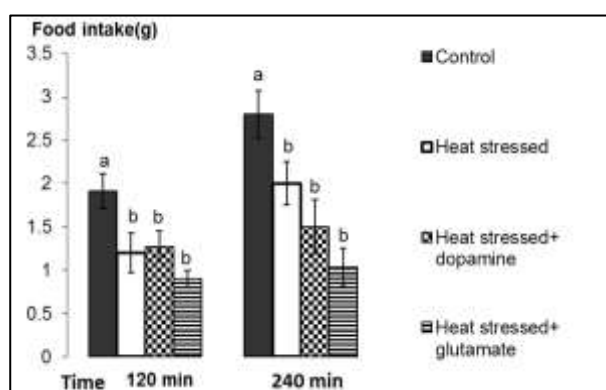


Figure 1: cumulative food intake of quails after intraperitoneal administration of apomorphine and glutamate. Different letters (a,b) indicates statistically significance between groups ( $P < 0.05$ )

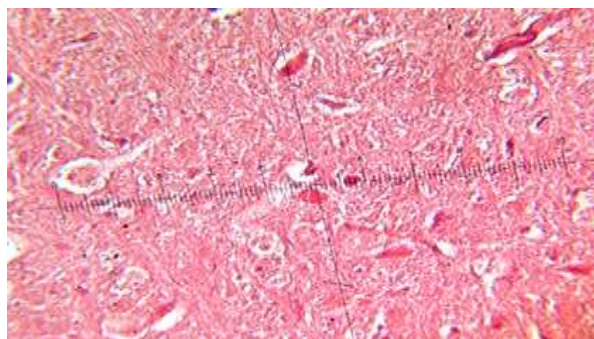


Figure 2: brain micrograph of a quail from the control group showing normal histological appearance. Hematoxylin and eosin staining  $\times 40$



Figure 3: brain micrograph of a quail exposed to heat stress showing enlargement of brain sinusoids (arrow). Hematoxylin and eosin staining  $\times 40$

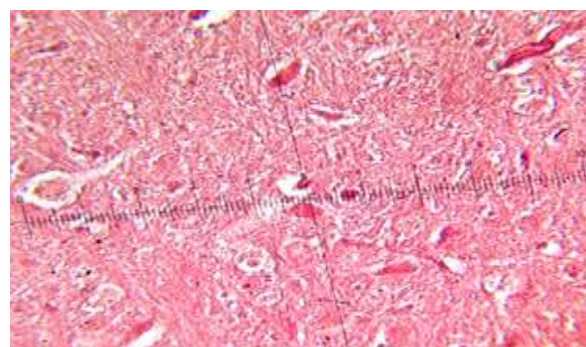


Figure 4: brain micrograph of a quail exposed to heat stress and treated with apomorphine. A decrease in enlargement of brain sinusoids (arrow). Hematoxylin and eosin staining  $\times 40$

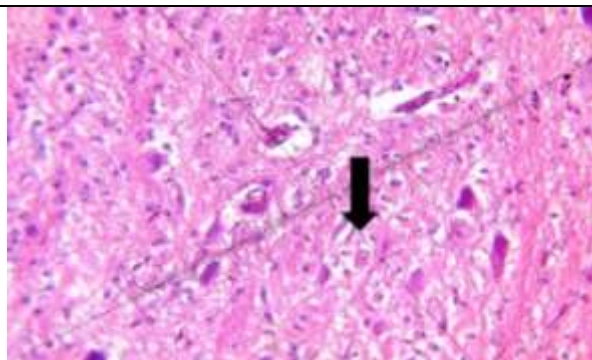


Figure 5: brain micrograph of a quail exposed to heat stress and treated with glutamate. An increase in neuronal damage and distention of blood sinusoids (arrow). Hematoxylin and eosin staining  $\times 40$

## Discussion

The changes in food intake and brain histology in heat treated quails treated with dopamine suggests that heat stress could affect food intake via dopaminergic pass ways which were in line with previous studies (17, 18). In the mammals, it seems that two major hypothalamic pathways are the predominant mediators of isoproterenol's influence on energy balance one involves the glutamate pathway and the other involves the dopaminergic neurons (19, 20). It is well known that the direct glutamate-induced activation of neuropeptide Y neurons in the ventromedial arcuate nucleus is paralleled by an inhibitory synaptic effect on  $\alpha$ -melanocyte stimulating hormone neurons of the ventrolateral arcuate nucleus (21).

The central anorexigenic effect of N/OFQ in birds isn't well understood but recent studies suggest that glutamate affects food intake in a manner similar to opioid peptides (22). Furthermore, both dopaminergic and glutamatergic receptors, has been shown to exist in peripheral nervous system and different parts of the chicken brain. (23). However, the sites within the quail brain that are involved in the action of these receptors, and moreover their interaction, needs to be fully clarified. The findings of the present study propose that dopamine receptors have modulatory effect on feed consumption and brain histology in quails. One possibility is that the modulatory effect of dopamine in quails may involve reduction in the glutamate content but further works would be necessary to be carried out. On the basis of these findings, it can be concluded that IP injection of glutamate induces a hypophagia in quails by reduction in the dopamine content. It is important to consider the mechanisms of food intake regulation in quails. Genetic selection has resulted in a dramatic increase of body weight of quails with. Therefore, most of the increase in growth rate must be related to changes in food intake rather than food efficiency.

These results indicate that both glutamate and dopamine receptors could have interactions in appetite regulation. This conclusion may be overturned by further research so more experiments should be carried out to examine the possible effect of dopamine receptor agonists. The effect of beta 1, beta 2 and beta 3-receptors and the interaction between dopamine and glutamate, especially in central nervous system, would also be the potential subjects for further studies.

## Ethical issue

The Author is aware of, and comply with, best practice in publication ethics specifically with regard to authorship (avoidance of guest authorship), dual submission, and manipulation of figures, competing interests and compliance

with policies on research ethics. Authors adhere to publication requirements that submitted work is original and has not been published elsewhere in any language. The experimental procedure was performed in accordance with the guidelines of work with laboratory animals, approved by the ethical committee of faculty of veterinary medicine. (IR.UOZ.REC.1398.3).

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The present study was performed at the animal laboratory center of University of Zabol.

## Authors' contribution

The author of this study have a complete contribution for data collection, data analyses and manuscript writing.

## Conflict of interests

The author declares that there is no conflict of interest.

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