EFFECTS OF INJECTION OF SEROTONIN INTO NUCLEUS CAUDATUS ON FOOD AND WATER INTAKE AND BODY WEIGHT IN ALBINO RATS

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Abstract : Serotonin is known to inhibit food and water intake. However, the effect of its injection into nucleus caudatus on food and water intake is not known. In the present study, serotonin hydrochloride, buspirone (the serotonin 5-HT_{1A} agonist) and ondensetron (the 5HT_3 antagonist) were injected into nucleus caudatus through stereotaxically implanted cannulae in three different dosages (1, 2 and 5 µg) and their effects on 24 h food and water intake, and body weight were recorded. The injection of serotonin hydrochloride resulted in a dose- dependent decrease in food intake attaining maximum of 27.3% at 5 µg dose, whereas water intake and body weight were decreased 12% and 4.3% respectively only at the highest does. Buspirone elicited a dose dependent inhibition of food and water intake and body weight (22.3%, 19.8% and 5.1% respectively), whereas ondensetron elicited an increase in food and water intake (37.8% and 36.3% respectively) without significantly altering bodyweight. It was concluded that serotonin hydrochloride injected into nucleus caudatus inhibits food and water intake significantly. These effects are mediated via 5-HT_{1A} and 5HT_3 receptors. The effect of injections of 5-HT_{1A} receptor agonist is more pronounced on water intake. The effect of injections of 5HT_3 receptor antagonist is also more pronounced on water intake.

Key words : serotonin   buspirone   ondensetron   nucleus caudatus
               food intake   water intake   body weight

INTRODUCTION

Serotonin has long been implicated in the control of food and water intake. Generally, it has been observed that injection of serotonin into different areas of the brain decreases food intake (1–5). It has also been observed that injection of various serotonin antagonists increases food intake (6–10). However, reports are also conflicting on the action of serotonin on ingestive behaviors. It is reported that 5-HT_{1A} receptor agonist increases food intake (11–16). It is also reported that 5-HT_3 antagonist, ondensetron injected intraperitoneally decreases food intake (16, 17). Thus, the

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action of agonists and antagonists of serotonin on ingestive behaviors is contradictory.

Injection of 8-OH-DPAT, serotonin 1A receptor agonist produces reduction in polydipsia and anorexia (18, 19). Injection of serotonin into paraventricular nucleus (PVN) of hypothalamus inhibits feeding by unknown mechanisms. It was proposed that serotonin induced anorexia (20). The suppressive effect of serotonin on carbohydrate intake was attenuated by injection of mianserin, $5-HT_{2A}$ antagonist. Intraperitoneal injection of fenfluramine results in depression of food intake. Chronic treatment with citalopram, a selective serotonin reuptake inhibitor, decreases both food intake and bodyweight gain in well nourished rats (21). It is suggested that effect of serotonin on food intake is mediated primarily via $5-HT_{1A}$ and $5-HT_{2c}$ receptors (4, 19). Both these receptor-subtypes are expressed in hypothalamic regions that are involved in regulation of feeding behaviors. Agents that activate $5-HT_{2c}$ and $5-HT_{1B}$ receptors produce hypophagia which indicate that serotonin through these receptors decreases food intake (22). Though injection of 8-OH-DPAT, $5-HT_{2A}$ agonist 15 minutes before refeeding of starved animals decreases food intake, injection of the same chemical after one hour of the start of refeeding, increases food intake (11). This indicates that serotonin has strong influence on food intake. However, the effect of 8-OH-DPAT on water intake was negligible in water-deprived animals.

Buspirone, $5-HT_{1A}$ agonist injected subcutaneously fifteen minutes prior to presentation of food produced a dose related inhibition of food intake in food deprived rats (3). It was suggested that inhibition of food intake in food-deprived rats was not due to non-specific disruption of behavior, rather due to the specific action of chemical on specific neural centers. However, it was also observed that regardless of the route of administration, buspirone increases food intake in a dose dependent manner for almost two hours from the start of presentation of food. Therefore, the role of buspirone on food intake is also found to be contradictory (in one experimental setting it decreases and in other setting it increases). It is also observed that buspirone, selectively increases food intake when the diet is rich in carbohydrate (13). Injection of low dose of 8-OH-DPAT is also observed to increase food intake (23). Thus, the effect of serotonin on same receptors studied by different investigators is found to be conflicting in nature.

Mesolimbic structures are strongly involved with regulation of behavioral functions (24). Nucleus caudatus, being a mesolimbic structure is also involved in the regulation of food and water intake in rats as reported from our laboratory (25–28). However, effect of injection of serotonin in nucleus caudatus on ingestive behaviors has not been studied yet. Moreover, $5-HT_{1A}$ and $5-HT_3$ receptors mainly mediate the effects of serotonin on ingestive behaviours. Therefore, in the present study we have assessed the role of serotonin, buspirone ($5-HT_{1A}$ agonist) and ondensetron ($5-HT_3$ antagonist) injected into nucleus caudatus on food and water intake and body weight in rats.

METHODS

A total number of 24 male albino rats of Wistar strain were taken for this study. They were about six months old with body weight ranging between 200–250 g. All animals were kept in separate cages. Food and water were provided ad lib.

Animals were allowed one week to recover from isolation stress, after which experiments were carried out. The temperature of the room in which animals were caged was between 28 to 32°C. Animals were exposed to 24 h natural light – dark cycle.

Measurement of basal food and water intake and body weight

Food and water were provided at 1400 h everyday, following which 24 h food and water intake were measured for each animal. For water intake, tap water at room temperature (30°C) was provided in calibrated glass cylinder having a metal spout. The minimum amount of change in water intake that could be recorded accurately was 0.5 ml. The food was provided in the form of standard rodent chow. Measurement of food was done by electronic weighing machine in which minimum change of 0.01 g could be recorded. The basal daily food and water intake were recorded on seven consecutive days to determine the 24 h basal mean food and water intake of each animal. Body weight of rats was recorded using electronic weighing machine. Basal body weight was obtained as the average of seven days recording.

Cannulation of nucleus caudatus

Cannulae were made by appropriately cutting the stainless steel injection needles of 20 G size. During cannulation of nucleus caudatus, animals were anaesthetized by intraperitoneal administration of Ketamine Hydrochloride (100 mg per kg body weight). Cannulations were performed by stereotaxic method using the co-ordinates of Konig and Klippel (29), following the procedures as described earlier (27).

Cannulations were performed unilaterally on the right side in all animals of all groups. Cannulae were allowed to remain in the brain for injecting chemicals till the animals were sacrificed. After cannulation, five days were given for the animal to recover completely and during the period animal was closely monitored for any infection. In our study there was no postoperative infection at all.

Preparation of dosages of chemicals

Serotonin hydrochloride (Lancaster, U. K.), was diluted in ethanol to prepare concentrations of 1 μg, 2 μg and 5 μg per μL respectively. Similarly, Buspirone (Rankem, New Delhi), a $5HT_{1A}$ receptor agonist, was diluted in ethanol to prepare concentrations of 1 μg, 2 μg and 5 μg per μL respectively and Ondensetron (Rankem, New Delhi), a $5HT_3$ receptor antagonist was diluted with ethanol to make 2 μg and 5 μg per μL solutions.

Experimental protocol

All the animals (24 totally) were divided equally into four groups with six animals

in each group. Group I was the serotonin group, Group II was the agonist group, Group III was the antagonist group and Group IV was the control group. Their 24 h basal food intake, water intake and body weight were measured before injection of chemicals.

Group I

In this group, different doses of serotonin hydrochloride (1 μg, 2 μg and 5 μg) were injected separately into nucleus caudatus of all six animals of Group I, on every alternate day and their 24 h food intake, water intake and body weight were measured following each injection. The schedule of injection was such that 1 μg was injected on Day 1, no injection was given on Day 2, 2 μg was injected on Day 3, no injection was given on Day 4, 5 μg was injected on Day 5, and no injection was given on Day 6, and so on and so forth till each dose of serotonin was injected on six occasions. Mean of these six recordings of each parameter was obtained as experimental post-injection values. These values were compared with their basal values and with the values of control animals.

Group II

In this group, different doses of buspirone (1 μg, 2 μg and 5 μg), $5-HT_{1A}$-receptor agonist, were injected separately into nucleus caudatus of all six animals of Group II. The protocol was otherwise identical to that employed in Group I.

Group III

In experiment 2, the maximally effective doses of buspirone were found to be 2 μg

and 5 μg per μL. Therefore, in this experiment 2 μg and 5 μg per μL doses of ondensetron, a $5-HT_3$ receptor antagonist, was injected into nucleus caudatus in animals of Group III.

In Group IV, the control group, equal amount (1 μL) of vehicle (ethanol) without drug was injected every alternate days into nucleus caudatus like that of experimental animals and their 24 h food intake, water intake and body weight were recorded and compared with their basal values.

Confirmation of cannulation

After completion of all the experiments, the animals were sacrificed and their brains were fixed by perfusing with 10% formalin solution. After perfusion, brains were removed for sectioning, staining and confirmation under microscope, which were performed by the procedures as described earlier (27).

The observations were recorded in all three groups and the obtained results were analyzed by one-way ANOVA, following which the level of significance was tested by paired 't' test.

RESULTS

Group I

The mean basal food intake, water intake and body weight in this group of animals were 11.37 ± 0.62 g, 26.1 ± 1.03 mL and 210.25 ± 2.58 g respectively. After injection of different doses of serotonin hydrochloride, there was significant and dose-dependent decrease in food intake of

TABLE I : Effect of injection of serotonin hydrochloride (SH) into nucleus caudatus on food intake (FI), water intake (WI) and body weight (BW) in rats (n = 6).

SH-Dose	FI (g)	WI (mL)	BW (g)
0 μg (Basal#)	11.37±0.62	26.1±1.03	210.25±2.58
1 μg	9.85±0.68* (–13.4%)	25.83±0.99 (–1.0%)	209.78±1.94 (–0.2%)
2 μg	9.66±0.62* (–15.0%)	24.41±0.67 (–6.5%)	206.3±1.23 (–1.9%)
5 μg	8.26±0.4*** (–27.4%)	22.96±0.49* (–12%)	201.18±1.05** (–4.3%)

*P<0.05; **P<0.01; ***P<0.001.

#Basal indicates values recorded before injection of serotonin hydrochloride.

Values in brackets indicate % decrease from the basal value.

TABLE II : Effect of injection of buspirone (BS), 5-HT_{1A} agonist into nucleus caudatus on food intake (FI), water intake (WI) and body weight (BW) in rats (n = 6).

BS-Dose	FI (g)	WI (mL)	BW (g)
0 μg (Basal#)	22.46±0.81	32.58±0.94	225.50±1.86
1 μg	21.71±0.86 (–3.3%)	29.14±0.78* (–10.5%)	220.46±1.92 (–2.2%)
2 μg	19.42±0.56** (–13.5%)	28.58±0.66** (–12.2%)	218.68±1.42* (–3.0%)
5 μg	17.46±0.84*** (–22.3%)	26.12±0.7*** (–19.8%)	213.82±1.10** (–5.1%)

*P<0.05; **P<0.01; ***P<0.001.

#Basal indicates values recorded before injection of buspirone.

Values in brackets indicate % decrease from the basal value.

animals (Table I). However, significant decrease in body weight and water intake was observed only at 5 μg dose of serotonin.

Group II

The mean basal food intake, water intake and body weight in this group of animals were 22.46 ± 0.81 g, 32.58 ± 0.94 mL and 225.50 ± 1.86 g respectively. After injection of 1 μg of buspirone, serotonin 5-HT_{1A} receptor agonist, there was significant decrease in water intake without significant change in food intake and body weight (Table II). However, with injection of higher doses of buspirone, there was significant and dose-dependent decrease in food intake, water intake and body weight of animals.

Group III

The mean basal food intake, water intake and body weight in this group of animals were 18.64 ± 0.78 g, 31.16 ± 0.55 mL

and 221.58 ± 1.98 g respectively. There was a significant increase in food and water intake following injection of 2 μg dose of ondensetron. The increase in water intake was proportionately greater than the increase in food intake. At 5 μg dose of ondensetron, there was highly significant increase in both the food and water intake (Table III). However, at both the doses, no change in body weight was observed.

TABLE III : Effect of ondensetron (ON), 5HT_3 antagonist on food intake (FI), water intake (WI) and body weight (BW) in rats (n = 6).

ON-Dose	FI (g)	WI (mL)	BW (g)
0 μg (Basal#)	18.64±0.78	31.16±0.55	221.58±1.98
2 μg	21.45±0.38* (+15%)	38.83±0.46*** (+24.6%)	223.64±2.12 (+0.9%)
5 μg	25.68±0.52*** (+37.8%)	42.46±0.84*** (+36.3%)	225.12±2.10 (+1.6%)

*P<0.05; ***P<0.001

#Basal indicates values recorded before injection of ondensetron.

Values in brackets indicate % increase from the basal value.

TABLE IV : Effect of injection of 1 µL of ethanol on food
intake (FI), water intake (WI) and body
weight (BW) in control rats (n = 6).

Ethanol volume	FI (g)	WI (mL)	BW (g)
(Basal[#])	21.82±0.74	29.92±0.67	218.72±1.74
1 µL	20.90±0.81 (–4.2%)	30.18±0.72 (+0.9%)	216.40±1.82 (–1.1%)

[#]Basal indicates values recorded before injection
of vehicle (ethanol).
Values in brackets indicate % increase from the
basal value.

In control animals, no significant change
in above-mentioned parameters was
observed following injection of equal volume
(1 µL) of vehicle (ethanol) into nucleus
caudatus when compared with their basal
values (Table IV).

DISCUSSION

In our study, injection of serotonin
hydrochloride into nucleus caudatus
resulted in decrease in food intake in a dose
dependent manner, which indicates that
serotonin in nucleus caudatus inhibits
feeding. Furthermore, injection of buspirone,
5-HT_{1A} agonist decreased food intake. This
indicates that serotonin acting via 5-HT_{1A}
receptors inhibits feeding. This is
contradictory to the observations of other
workers who have demonstrated that
buspirone increases feeding behavior (12–
14). They have demonstrated that buspirone
not only increases food intake, it increases
it in a dose dependent manner irrespective
of its route of administration (12). It was
also observed that buspirone selectively
increases food intake when food is rich
in carbohydrates (13). However, our
findings agree with the findings of other
investigators, who have demonstrated

that buspirone inhibits food intake in a
dose dependent manner (3, 4). It was
also further revealed that buspirone
inhibits food intake partly by stimulating
the release of dopamine in the brain,
which is a known inhibitor of feeding
behavior (30).

Our study also supports the findings of
other workers in which 5-HT_{1A} agonists
other than buspirone, like ipaspirone have
been shown to inhibit food intake (15, 18).
Therefore, it can be concluded that serotonin
inhibits food intake via 5-HT_{1A} receptors.
However, inhibition of food intake by
buspirone in our study was observed only
at higher doses. Moreover, injection of
ondansetron, 5-HT_3 antagonist stimulated
food intake. This clearly indicates that
serotonin normally inhibits feeding
behavior, which also is mediated via 5-HT_3
receptors.

In our study, serotonin also inhibited
water intake, though only at the highest
dose. However, the inhibition of water
intake by buspirone was significant even at
the lower dose, and buspirone inhibited
water intake in a dose dependent manner.
These findings, that no significant decrease
in water intake inspite of significant
decrease in food intake following injections
of 1 and 2 µg doses of serotonin, and
significant decrease in water intake inspite
of no significant decrease in food intake at
1 µg dose of buspirone, indicate that the
inhibition of water intake was independent
of inhibition of food intake. Since the
hypodipsia induced by these chemicals was
independent of hypophagia, it is suggested
that serotonin induced hypodipsia may a
type of "primary hypodipsia".

Following injections of buspirone, there was also a dose dependent decrease in body weight. No significant change of body weight was observed at 1 µg dose. But, at 2 µg dose of buspirone, decrease in body weight was significant and was further significantly decreased at 5 µg dose of buspirone. It is proposed that separate centers in the brain exclusively control body weight independent of food intake (31). Nucleus tractus solitarius (NTS) and ventromedian hypothalamus (VMH) are the proposed ponderostats (centers controlling body weight). It has also been proposed that separate neurotransmitter systems in the brain control regulation of body weight. These neurotransmitters are called ponderostatic neurotransmitters.

Injection of ondansetron, 5-HT_3 receptor antagonist increased food intake in a dose dependent manner. This further substantiates the earlier finding that serotonin inhibits food intake as its antagonist increases food intake. It also can be well concluded that the inhibitory effect of serotonin was mediated via 5-HT_3 receptors, in addition to its action through 5-HT_{1A} receptors. Injection of ondansetron resulted in increased water intake significantly even at the dose of 2 µg ($P<0.001$), the dose at which increase in food intake was just significant ($P<0.05$). This again suggests that water intake induced by serotonin antagonist is independent of increased food intake.

Inspite of increase in food and water intake, there was no significant increase in body weight following injections of ondensetron. This indicates that body weight is not solely dependent on ingestive behaviors. Though the injection of buspirone, 5-HT_{1A} agonist resulted in decrease in body weight, injection of ondansetron, 5-HT_3 antagonist, did not elicit significant increase in body weight. This shows that serotonin antagonist do not influence body weight though they increase food intake. It further indicates that neural mechanisms controlling body weight may be separate from the neural mechanisms controlling food intake. However, it could also be argued that the significant change in body weight was not observed as the study was a short-term study of injections of chemicals. Therefore, a long-term study should be taken up to assess the role of serotonin on change in body weight, which we plan in our future studies.

In our previous experiments, we have observed that lesion of nucleus caudatus results in decreased food and water intake and injections of catecholamines and angiotensin into nucleus caudatus increases food and water intake (25–28, 32). This shows that nucleus caudatus is an important element of neural circuitry involved in the regulation of ingestive behaviors. Injection of various chemicals into nucleus caudatus changes food and water intake without producing significant motor abnormalities as we have observed in our previous studies and also in the present study. This indicates that nucleus caudatus is an important structure that solely influences feeding and drinking behavior in rats. In the present study, as we observed that injections of serotonin agonist and antagonist into the same nucleus alter ingestive behaviors, we conclude that nucleus caudatus is an important centre in the brain controlling

these physiological parameters. Serotonin and serotonin 5-HT$_{1A}$ receptor agonist (buspirone) decreased food and water intake and body weight, whereas serotonin 5-HT$_3$ receptor antagonist (ondensetron) increased these parameters. It was concluded that serotonin injected into nucleus caudatus inhibits ingestive behaviors and these effects of serotonin are mediated by 5-HT$_{1A}$ and 5-HT$_3$ receptors. It needs further studies of confirm the role of serotonin in nucleus caudatus on the regulation of body weight.

ACKNOWLEDGEMENTS

REFERENCES

1. Sugimoto Y, Yoshikawa T, Yamada J. Effects of peripheral administration of 5-hydroxytryptamine (5-HT) on 2-deoxy-D-glucose-induced hyperphagia in rats. *Biol Pharm Bull* 2002; 25(10): 1364–1366.

2. Ruibal C, Soengas JL, Aldegunde M. Brain serotonin and the control of food intake in rainbow trout (Oncorhynchus mykiss) : effects of changes in plasma glucose levels. *J Comp Physiol (A Neuroethol Sens Neural Behav Physiol)* 2002; 188(6): 479–484.

3. Ebenezer IS. Effects of buspirone on operant and nonoperant food intake in food deprived rats. *Methods Find Exp Clin Pharmacol* 1996; 18(7): 475–480.

4. Montgomery AM, Rose IC, Herberg LJ. 5-HT$_1$A agonists and dopamine : the effects of 8-OH-DPAT and buspirone on brain-stimulation reward. *J Neural Transm Gen Sect* 1991; 83(1–2): 139–148.

5. Mancilla-Diaz JM, Escartin-Perez RE, Lopez-Alonso VE, Cruz Morales SE. Effect of 5-HT in mianserin-pretreated rats on the structure of feeding behavior. *Eur Neuropsychopharmacol* 2002; 12(5): 445–451.

6. Cooper SJ, Greenwood SE, Gilbert DB. The selective 5-HT$_3$ receptor antagonist, ondensetron, augments the anorectic effect of d-amphetamine in nondeprived rats. *Pharmacol Biochem Behav* 2002; 45(3): 589–592.

7. Shankar RP, Karan RS, Handu SS, Bhargava VK. Effect of the 5-HT$_3$ receptor antagonist ondensetron on amphetamine-induced hyperactivity and stereotype in rats. 5: *Indian J Physiol Pharmacol* 2000; 44(3): 355–358.

8. Higgins GA, Tomkins DM, Fletcher PJ, Sellers EM. Effect of drugs influencing 5-HT function on ethanol drinking and feeding behaviour in rats : studies using a drinkometer system. *Neurosci Biobehav Rev* 1992; 16(4): 535–552.

9. Dourish CT, Clark ML, Fletcher A, Iversen SD. Evidence that blockade of post-synaptic 5-HT$_1$ receptors elicits feeding in satiated rats. *Psychopharmcology (Berl)* 1989; 97(1): 54–58.

10. Voigt J, Schade R, Fink H, Hortnagl H. Role of 5-HT$_1$A receptors in the control of food intake in obese Zucker rats of different ages. *Pharmacol Biochem Behav* 2002; 72(1–2): 403–409.

11. Saadoun A, Cabrera MC. Effect of the 5-HT (1A) receptor agonist 8-OH-DPAT on food and water intake in chickens. *Physiol Behav* 2000; 75(3): 271–275.

12. Li ET, Luo S. Buspirone-induced carbohydrate feeding is not influenced by route of administration and nutritional status. *Brain Res Bull* 1993; 30(5–6): 547–550.

13. Luo SQ, Ransom T, Li ET. Selective increase in carbohydrate intake by rats treated with 8-hydroxy-2-(di-n-propylamino)-tetraline or buspirone. *Life Sci* 1990; 46(23): 1643–1648.

14. Aulakh CS, Hill JL, Murphy DL. A comparison of feeding and locomotion responses to serotonin agonists in three rat strains. *Pharmacol Biochem Behav* 1988; 31(3): 567–571.

15. Gilbert F, Dourish CT. Effects of the novel anxiolytics gespirone, buspirone and ipsapirone on free feeding and on feeding induced by 8-OH-DPAT. *Psychopharmacology (Berl)* 1987; 93(3): 349–352.

16. van der Hoek GA, Cooper SJ. Ondernsetron, a selective 5-HT$_3$ receptor antagonist, reduces palatable food consumption in the nondeprived rats. *Neuropharmacology* 1994; 33(6): 805–811.

17. Mazzola-Pomietto P, Aulakh CS, Murphy DL. Temperature, food intake, and locomotor activity effects of 5-HT$_3$ receptor agonist and two 5-HT$_3$ receptor antagonists in rats. *Psychopharmacology (Berl)* 1995; 121(4): 488–493.

18. Ryan CN, Evenden JL, Petterson M. Effects of buspirone and ipsapirone on schedule induced polydipsia : comparison with 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) and raclopride. *Psychopharmacology (Berl)* 1993; 112(1): 34–44.

19. von Meyenburg C, Langhans W, Hrupka BJ. Evidence for a role of the 5-HT(2C) receptor in central lipopolysaccharide-, interleukin-1beta-, and leptin-induced anorexia. *Pharmacol Biochem Behav* 2003; 74(4): 1025–1031.

20. Helm KA, Rada P, Hoebel BG. Cholecystokinin combined with serotonin in the hypothalamus limits accumbens dopamine release while increasing acetylcholine : a possible satiation mechanism. *Brain Res* 2003; 14: 963(1–2): 290–297.

21. Barreto Medeiros JM, Cabral Filho JE, De Souza SL, Freitas Silva SR, Mendes Da Silva C, Deiro TC, Monteiro JM, Guedes RC, De Castro CM, Manhaes De Castro R. Early malnourished rats are not affected by anorexia induced by a selective serotonin reuptake inhibitor in adult life. *Nutr Neurosci* 2002; 5(3): 211–214.

22. Schreiber R, De Vry J. Role of 5-HT2C receptors in the hypophagic effect of m-CPP, ORG 37684 and CP-94,253 in the rat. *Prog Neuropsychopharmacol Biol Psychiatry* 2002; 26(3): 441–449.

23. Dourish CT, Hutson PH, Curzon G. Low doses of the putative serotonin agonist 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT) elicit feeding in the rat. *Psychopharmacology (Berl)* 1985; 86(1–2): 197–204.

24. Patton HD, Fuchs AF, Hille B, Scher M, Steiner R. The limbic system. *Text Book of Physiology*, Volume 1, (W. B. Saunders Co.) 1989; 701–756.

25. Pravati Pal, Pal GK, Madanmohan and Srinivasan V. A study of the effect of angiotensin injected into nucleus accumbens and caudatus on feeding and drinking behavior in rats. *Biomedicine* 1999; 19(3): 191–198.

26. Pal P, Pal GK, Madanmohan, Srinivasan V. Effect of dopamine and angiotensin injected into nucleus accumbens and caudatus on food and water intake in rats. *Biomedicine* 2000; 20(1): 17–26.

27. Pal GK, Bharathi, Thombre DP. Modulation of daily water intake by dopamine in caudate and accumbens nuclei in rats. *Physiol Behav* 1992; 51: 851–856.

28. Pal GK. Pravati Pal, Selvam SR Raj, Madanmohan. Modulation of feeding and drinking behavior by catecholamine injected into nucleus caudatus in rats. *Indian J Physiol Pharmacol* 2001; 45(2): 172–180.

29. Konig FR, Klippel AR. The Rat Brain; A Stereotaxic Atlas of the Forebrain and Lower parts of the Brainstem. The Williams and Wilkins Co. 1963.

30. Gobert A, Rivet JM, Cistarelli JM, Millan MJ. Buspirone enhances duloxetine- and fluoxetine-induced increases in dialysate levels of dopamine and noradrenaline, but not serotonin, in the frontal cortex of freely moving rats. *J Neurochem* 1997; 68(3): 1326–1329.

31. Cabanac M, Duckloux R, Spector NH. Sensory feed in the regulation of body weight. Is there a ponderostat ? *Nature* 1971; 229: 125–127.

32. Thombre DP, Krishnamurthy N, Pal GK. Effect of different schedules on food intake in caudate lesioned rats. *Indian J Physiol Pharmacol* 1994; 38(4): 313–315.