Summary
The present study was undertaken to investigate both ovariectomy and estradiol benzoate (EB) induced changes in food intake (FI), water intake (WI) and body weight (BW) and to elucidate the possibility of a role for dopamine receptors in mediating such changes in ventromedial hypothalamus (VMH), nucleus septal lateralis (NSL) and basolateral amygdala (BLA) that play a crucial role in the control of ingestive behaviors and body weight. Ovariectomy induced changes in ingestive behaviors and body weight were assessed by injecting EB (estradiol benzoate), SKF and BC (dopamine D1 and D2 receptor agonists, respectively) into VMH, NSL and BLA. The role for specific dopamine receptor that mediates EB effects on daily FI, WI and BW was investigated by blocking dopamine D1 and D2 receptors in VMH, NSL and BLA with SCH and sulpiride (dopamine D1 and D2 receptor specific antagonists, respectively). The following were the major findings from the present study.

- Transient increase in FI and WI with sustained elevation of BW was observed following bilateral ovariectomy in female rats compared to sham operated controls.

- Conversely, EB substitution (central injections) has inhibited the ovariectomy induced transient increase in FI, WI and sustained elevation of BW in VMH, NSL and BLA.

- These transient changes (increase or decrease) in FI and WI, following ovariectomy and EB substitution may be an attempt to overcome the sustained changes (increase/decrease) in BW. Further, given the paucity of literature with respect to
actions of EB in NSL and BLA, the finding that direct injection of EB into these nuclei suppressed ingestive behaviors and BW, was novel and interesting.

- Following central administration of the EB, the decrease in FI, WI and BW was predominant in VMH compared to NSL and BLA, and this may be owing to the fact that VMH contains high density of estrogen-binding and estrogen sensitive neurons than NSL and BLA.

- Following ovariectomy, subcutaneous administration of EB exerted significant inhibitory effects on FI, WI and BW when nuclei (VMH, NSL and BLA) were intact compared to vehicle injected controls. Due to its lipophilic nature, EB would expect to cross the blood brain barrier and diffuse to the CNS and there it can act on estrogen receptors present in multiple regions of the brain and this would probably had additive effect on these measures. Therefore, there was no difference in the magnitude of inhibition of FI, WI and BW in any group, following subcutaneous EB treatment with intact nuclei.

- Rats with VMH, NSL and BLA lesions displayed smaller additional increase in FI, WI and BW compared to sham lesions, following ovariectomy. Conversely, rats with lesions showed slight reduction in FI, WI and BW, following subcutaneous injection of EB. Moreover, the magnitude of decrease in FI and BW was far less in rats with VMH lesions compared to NSL and BLA lesions. Taken together the present findings suggest that usually the receptors present in these nuclei monitor estrogen
and affect FI, WI and BW and destruction of these receptors with lesions might reduce the influence of EB on these measures.

- Central administration of bromocriptine (D2 receptor agonist) was equally effective in the inhibition of FI and BW akin to EB, following ovariectomy. The effect of SKF (D1 receptor agonist) was less compared to bromocriptine. In general, the magnitude of inhibition in FI and BW induced by EB and bromocriptine in VMH was comparable to NSL and greater than BLA. While, SKF induced suppression on WI predominantly seen in VMH and BLA. The observed effects of bromocriptine on FI and BW may be in part due to presence of abundant D2 receptors in VMH and NSL compared to BLA.

- In OVX (ovariectomized) rats, EB has prevented predominantly sulpiride (dopamine D2 receptor antagonist) induced increase in FI and BW and SCH (D1 receptor antagonist) induced WI. It appears that the EB induced inhibition of FI and BW in ovariectomized rats, predominantly mediated by D2 receptors and WI mainly by D1 receptors. The degree of prevention of EB on sulpiride induced changes in FI and BW was considerably high in VMH and NSL than BLA.

- In NSL, D1 and D2 receptors had shown predominant effect on BW and FI, similar to VMH. However, neither D1 and D2 agonists nor D1 and D2 antagonists had effect on WI, suggesting that dopamine may not be candidate neurotransmitter in the regulation of WI in NSL.
Limitations

This study has several limitations that preclude the possibility of interpreting how exactly estradiol and dopamine receptors are involved in the regulation of ovariectomy induced ingestive behaviors and body weight in VMH, NSL and BLA.

- Present findings demonstrate that both dopamine D1 and D2 receptors contribute in the pathophysiology of ovariectomy induced hyperphagia and obesity and also in EB mediated actions mainly on FI and BW. Therefore, further research on the regulation of DA receptor expression in VMH, NSL and BLA with particular attention to D2 receptor is needed.

- Several local concentrations of neurotransmitters dopamine, norepinephrine, serotonin, NPY etc that play a crucial role in the control of ingestive behaviors and body weight, were not assessed.

- Hormone concentrations such as estrogen, insulin and neuromodulators like leptin involved in the regulation of ingestive behaviors and body weight, were not measured.

- In our present study, we have measured daily FI, along with WI and BW. However, daily food intake (FI), as a function of time, is the product of meal size (MZ) and meal number (MN) \([FI=MZ \times MN]\) that constitutes a feeding pattern, while MZ and MN are differentially affected by different manipulations. Ovariectomy increases MZ and decreases MN, while EB and dopamine treatment reverse this feeding pattern. Therefore feeding pattern is a better index to elucidate the neural controls of ingestive behavior, rather than cumulative daily FI.