SYNOPSIS AND OVERVIEW OF THE CONTRIBUTIONS OF THE STUDIES PRESENTED IN THE THESIS
1. Contributions from the double electrode assessment on the effects of lesions on the operant self-stimulation (SS) behaviour, biogenic amines and operant feeding behaviour.

The study of lesions revealed that relatively small size electrolytic lesions (bilateral) in the lateral hypothalamus (LH) have not affected the self-stimulation (SS) of substantia nigra-ventral tegmental area (SN-VTA). No effect was also observed in the converse experiment. i.e., the small size lesions in the SN-VTA caused no significant change in the SS of LH. This was interesting since the electrolytic lesion eliminates not only the dopaminergic or noradrenergic neuronal elements but also all the others in the site of lesion and hence also indirectly cause changes in other regions that are connected to the site of lesions. Some of the neuronal elements that were lost in the site were assumed to be concerned with the SS function of that region, because before making the lesions the property of SS of that region was tested and elicited on several days through the same electrode that was intended to be used subsequently to pass the current for making lesions. Since the lesions had abolished the SS through that electrode, but not of the second electrode located in the second region. The implication derived was that the two regions (LH and SN-VTA) have their own independent or semi-independent neural substrates of SS.

The effects of the small lesions made in the SS sites mentioned above have also been studied by estimating the levels of dopamine, norepinephrine and serotonin in different brain regions that are known to represent the major target sites of the projections of these neural systems. It was found that the above kind of small lesions made in the SS regions did not produce any significant reduction of dopamine, norepinephrine and serotonin in brain regions except in the site of lesion where the levels were down on an average. Since the loss of SS occurred despite the survival of the major part of the substrates of the three amines, it is assumed that the SS of these regions may not be so much dependent on these neuronal systems in the lesioned regions, but may be dependent on some other types of neuronal system.
In contrast to the above, the larger size lesions (bilateral) caused a reduction in the SS of the second site also. In this type of lesioned subjects, the levels of the dopamine, norepinephrine and serotonin were found to be reduced in different brain regions on an average by about 30 - 40%, besides in the lesioned regions. Hence, in these types large lesions, it is inferred that not only the SS substrates of the region but also monoaminergic neuronal substrates could have been non-specifically disrupted in the destruction caused by the larger lesions.

The operant responses for food reward (FR-5) were not affected by the small size lesions of the SS sites (bilateral) either in the LH or SN-VTA. Hence, it was inferred that the neural substrates subserving the feeding drive may be considerably separate from the neural substrates serving the SS function. However, large size lesions caused significant reduction in the operant responding for food reward. Hence, larger lesions might have encroached on both substrates namely of the SS as well as of the feeding functions of the region.

II. Contributions on the effects of catecholaminergic receptor ligands on operant SS behaviour and on single unit electrical activities of the regions of LH and SN-VTA.

a) Effects on operant SS and feeding behaviours.

Haloperidol (D₂ antagonist) at a dose of 0.05 mg/Kg, I.P.; apomorphine (DA agonist) 0.5 mg/kg, I.P.; yohimbine (α₂ antagonist) 5mg/Kg, I.P. and clonidine (α₂ agonist) 0.15 mg/Kg I.P. caused about 30-50% reduction of responding for SS from SN-VTA and LH. At these doses, the operant feeding behaviour was almost completely abolished. This implies that the drive and motivation for responding for SS was relatively less affected than that of the operant feeding behaviour by the catecholaminergic receptor modulators. Also, it was obvious that the impairment of the operants for feeding was not so much due to motor incapacitation, since the operants for SS were intact by about 60% of normal. It was probably due to reward value
reduction for food. The same kind of reasoning would suggest that the reduction of the 30-50% of the SS operant might be due to a partial blunting or impairment of the reward under these doses of the catecholaminergic receptor ligands. Support for these inference was also noted in the similarity of the time course of change of the operant responding observed after haloperidol to the extinction pattern. The effects might be due to the action of the ligands on receptors present in the regions of SS electrodes as well as in other regions of brain, since these drugs were administered systemically.

b) Effects on single unit electrical activities.

The doses similar to the above were injected into the subjects prepared under chloral hydrate anaesthetia in acute experiments. Haloperidol caused an increase of firing of units on an average upto 292% in SN-VTA and 417% in LH. Apomorphine caused a significant reduction upto about 85% in both the areas. There were no such studies previously reported on the LH units.

Clonidine caused a reduction upto 70-80% of control in firing rates of units of both the LH and SN-VTA. Yohimbine also caused a reduction of firing of roughly a similar magnitude in the firing of the both regions. No previous reports were available in the literature on the effects of the nor-adrenergic receptor ligands on the unit firing in LH and SN-VTA.

The studies suggested that any imbalance created in the receptor function either by the agonist or antagonist would lead to alterations in operant behaviours. However the sites of action of these drugs leading to the disturbances of unit activities could be also in other regions that project to SN-VTA and LH, as the systemic injections would be acting in all regions of the brain. Studies with local intracerebral injections would be required to differentiate local effect from those of other brain regions on the unit activities. This type of caution in the interpretation is imperative in view of the results observed with the lesions described above.
III. Alterations of single unit electrical activities by stimulation of one region on the other.

These experiments were also done on subjects anaesthetised using chloral hydrate. Electrical stimulation of LH using the same parameters as have been used in self-stimulation paradigm caused an increase of about 30-40% firing rates of 75% of the SN-VTA units studied. On the contrary, such stimulation of the SN-VTA region caused about 40-50% inhibition of firing rates of about 90% of the LH units studied. Thus, the results revealed that the two regions can exert interactions between them, but it can not be concluded that these types of interactions would be involved directly in the SS reward mechanisms of the two regions. The electrical stimulation currents could have also excited the other non-SS substrates of the regions. However, it can not also be suggested that no interactions operate between the two regions during SS behaviour. While separate substrates of SS could be existing in the two regions, there could also be some supplemental interactions between the two substrates. The lesion studies reported in the other sections of the thesis revealed that the neural substrates of SS of LH and SN-VTA could be operating fairly separately. Since these two areas (LH and SN-VTA) are known to be involved in regulating various other behaviours besides the SS, the possibility of the two regional interactions revealed by the unit data might also be relevant in achieving correlations in the other functions.

IV. Alterations of dendritic arborizations of neurons in the sites of self-stimulation and hippocampus.

The results revealed that a significant increase in the dendritic branching points in the perisomatic domains of the neurons of the SS regions following a 10 day experiencing of the SS. This type of change was observed in both LH and SN-VTA regions. The hippocampal CA3 neurons also showed a significant change, more in the apical dendritic branching than basal dendritic branching. This is the first time that such a study on neurons in the SS regions has been made and no such study has been reported in the previous
literature. The study brought the suggestion that there might be appropriate alterations induced by the SS reward experience in some of the brain areas, just as it has been demonstrated in other experiments in recent years that learning would induce both molecular and morphological changes in the participating neurons.

On the whole the observations presented in the thesis are consistent with the hypothesis of the SS behaviour having independent mechanisms in the LH and SN-VTA while there may be a basis for neuronal interactions between the two regional substrates. Furthermore, the responding for SS may lead to changes in dendrites and synapses of some areas of the brain. Studies with systemic administration of catecholaminergic agents showed that these cause alterations of unit activities of both the LH and SN-VTA and since these alterations could be due to secondary consequences of the actions of the drugs elsewhere in the brain, systemic administration studies cannot be relied to infer differences in the role of catecholaminergic receptors in the substrates of the two regions.