

CHAPTER 4

DISCUSSION

The present study clearly demonstrated that the nucleus accumbens received a wide varieties of afferent inputs. Following HRP injection in the nucleus accumbens labeled neurons were observed in many areas of telencephalon, diencephalon and brainstem. Although the afferent connections of the nucleus and their topographical organization have not been systematically studied prior to this investigation in the rat, most of the projections to the nucleus accumbens reported to date have noted in anterograde tracing experiments.

The ventral subiculum was shown to project to the rostral part of the nucleus accumbens (Figure 1, Plate 2). Similar finding has been reported by an autoradiographic technique in the rat (Swanson and Cowan, 1977). By contrast, Newman and Winans (1980) demonstrated by retrograde transport of HRP in the hamster that the entire subiculum projected to nucleus accumbens. More recently, Groenewegen et al, (1982) using fluorescent tracers combining with anterograde [^3H] leucine and [^{35}S] methionine suggested that subiculum projection to the nucleus accumbens appeared to be topographically organized in the cat. This discrepancy is probably due to species difference.

The projection from the hippocampal field CA1 to middle-medial part of the nucleus accumbens observed in the present study has been reported in the study using degeneration techniques in the cat, rat and monkey (Fox, 1943; Raisman et al, 1966; Siegel and Tassoni, 1971; de Olmos and Ingram, 1972; Siegel et al, 1975; Heimer and Wilson, 1975), as well as, in the study using HRP technique in hamster which showed that the intermediate portion of hippocampal field CA 1 send their axons to rostral nucleus accumbens (Newman and Winans, 1980). Heimer and Wilson (1975) demonstrated that hippocampus projection terminated in the caudal as well as rostral part of the nucleus accumbens. It was possible that the degeneration they observed in the caudal area following ablation of the rat hippocampus was due to the destruction of subiculum and entorhinal fibers-of-passage projecting to the caudal part of the nucleus through the fimbria (Newman and Winans, 1980)

Dopaminergic neurons in the ventral tegmental area and substantia nigra has been shown to project to the nucleus accumbens of rat, cat and rabbit (Fallon and Moore, 1978; Deniau et al. 1980; Ungerstedt, 1971; Beckstead et al. 1979 Chronister et al. 1980). The present study provided more details that neurons in the ventral tegmental area projected to all part of nucleus accumbens, while the substantia nigra, pars compacta, projected to the middle-medial part of the nucleus accumbens. On the contrary, Newman and Winans (1980) demonstrated that only ventral

tegmental area projected to all part of the nucleus accumbens. The absence of projections to nucleus accumbens from the substantia nigra in hamster might simply reflect differences in the topographical organization of the dopaminergic neurons in different species (Newman and Winans, 1980).

Many thalamic nuclei including parataenial nucleus, parafasicular nucleus, paraventricular nucleus, reuniens nucleus and medialis thalamic nucleus were shown to project to the nucleus accumbens in the present study. These projections were found in the rostral and middle-medial region of the nucleus accumbens. In additions the projection from the parataenial nucleus was also found in caudal region. These projections have been demonstrated, however, without specific sites of termination in the nucleus accumbens of rat, rabbit and monkey (Cowan and Powell, 1955; Powell and Cowan, 1956; Leonard, 1969; Swanson and Cowan, 1975; Herkham, 1978). Recent autoradiographic study with tritiated leucine and proline injected into the parataenial nucleus also demonstrated that parataenial nucleus projected to the entire antero-posterior extent of medial part of the nucleus accumbens (Kelley and Stinus, 1984).

Other areas reported to project to nucleus accumbens on the basis of degeneration techniques were entorhinal cortex of rat (Krayniak et al, 1981), dorsal raphe' of rat (Bobiller et al, 1966), interpeduncular nucleus of tamandua (Smith, 1930), These projections were also found in the present study with additional information that the

entorhinal cortex projected to middle-lateral part of the nucleus accumbens. Axons from dorsal raphe neurons terminated in rostral and middle-medial part of nucleus accumbens while the projection from the interpeduncular nucleus were confined in the rostral, middle-medial and caudal part of the nucleus.

The present study fails to demonstrate the projection from the olfactory cortex (de Olmos and Ingram, 1972), the anterior cingulate gyrus, rostral sulcal cortex and the perirhinal cortex (Groenewegen et al, 1980; Newman and Winans, 1980). As indicated previously by using HRP technique negative finding did not exclude the existence of such projections. The absence of these projection might be due to the possibility that some neuronal connections did not transport HRP.

The basolateral and basomedial amygdalo-accumbens projections found in the present study confirmed previous finding obtained from degeneration techniques in the rat and the cat (Cowan et al, 1965; Krettek and Price, 1978). The basomedial amygdalo-accumbens projections were reported absent in hamster (Newman and Winans, 1980). The authors noted that basomedial amygdala nucleus of hamster was poorly developed.

Based of the finding obtained from the present study, the nucleus accumbens received afferent connections from a number of limbic structures, including the amygdala,

the hippocampus and the subiculum and from the mesolimbic dopaminergic projection (ventral tegmental nucleus). Its efferents were shown project to the substantia nigra and ventral pallidum of the basal ganglia (Conrad and Pfaff, 1976; Nauta et al, 1978; Newman and Winans, 1980; Swanson and Cowan, 1975).

It may be speculated that limbic projections to the nucleus accumbens were functionally significant pathways by which limbic structures could influence the extrapyramidal system. On the other hand, the substantia innominata of which the ventral pallidum is considered to be a component were shown to project to the lateral hypothalamus and lateral habenula nucleus (Barone et al, 1981; Paikovits and Zaborszky, 1979). A projection from the amygdala to these areas would form a limbic-basal ganglia-limbic loop that may not be directly involved in somatic activity. A third possible efferent target of the ventral pallidum were shown to be the mesencephalic locomotor region (Grillner and Shik, 1973). Such a pathway may be plausible, since it may explain the locomotor hyperactivity in rats following injection of dopamine into the nucleus accumbens (Mogenson and Manchanda, 1979; Pijnenburg et al, 1976).

Recent electrophysiological study shown that the relay of output from amygdala to the ventral pallidum via the nucleus accumbens was under the modulating influence of the mesolimbic dopamine projection from the ventral

tegmental area (Yim and Mogenson, 1983) and the relation of this dopamine pathway to motor functions has also been demonstrated (Iversen and Koob, 1977; Mogenson et al, 1979; Pijnenburg et al, 1976). It has been suggested from behavioral study that dopamine in the nucleus accumbens may be important in the initiation of movement (Mogenson et al, 1980; Mogenson and Yim, 1981). And as the akinesia in Parkinson's disease patients could be related to depletion of dopamine in the nucleus accumbens (Price et al, 1978), this midbrain to telencephal dopamine projection could gate signal transmission in accumbens and modulate the influence of a limbic structure on the somatic activities.

Furthermore, Lopes da Silva et al, (1984) suggested that possibility of the pathways from subiculum and entorhinal cortex to the nucleus accumbens might provide the basis for a motor interface between limbic cortex and those systems responsible for programming and modulation of motor act.

Thalamic nuclei especially the paratenial nucleus were demonstrated to receive projection from prefrontal cortex and projected to the amygdala and hippocampus (Kelley and Stinus, 1984). Eventhough the functional relationship between limbic-thalamic and nucleus accumbens was unknown. Kelley and Stinus, (1984) suggested that parataenial nucleus could influence behavioral function of the nucleus accumbens.

The present study has provided an additional information that the afferent projections terminating in the nucleus accumbens are topographically organized; ie: afferent from limbic region terminate mainly in the rostral and middle part of the nucleus accumbens: termination of mesolimbic region distributes throughout the nucleus (most heavily in rostral and middle part of the nucleus accumbens).

The more interesting finding is that afferent projections tend to terminate in the rostral and middle part of the nucleus while the caudal part receives very few projections. Based on this findings, it may be suggested that rostral and middle parts of the nucleus are the sites of receiving informations from various sources. These informations may be integrated by the neuronal networks of the nucleus accumbens before sending to other areas of the brain (including the globus pallidus) via the neurons in the caudal part.

SUMMARY

The study of the afferent connections of the nucleus accumbens presented herein was based on the method of retrograde axonal transport of horseradish peroxidase (HRP)

Axons from neurons in the areas of ventral subiculum, hippocampal field CA1 and amygdaloid nucleus both pars basolateral and basomedial, of limbic terminated in the rostral and middle part of nucleus accumbens. Projections from ventral tegmental nucleus terminated in the whole part of the nucleus.

The thalamic nucleus fibers including parataenial nucleus, parafascicular nucleus, paraventricular nucleus reuniens nucleus and medialis thalamic nucleus appear to terminate along the rostral to middle-medial part of nucleus accumbens.

The afferent projections from other areas were the projections from entorhinal cortex to middle-lateral part and substantia nigra, pars compacta to middle-medial nucleus. In addition, most of the dorsal raphe fibers extended to the middle-medial part but a few ended in the rostral part of nucleus accumbens. The interpeduncular nucleus terminated diffusely with the entire of nucleus accumbens except the middle-lateral part. The projections found in this experiment were ipsilateral and were shown to

be topographically organized.

According to their distribution pattern, the afferent projections tended to terminate in the rostral and middle part of nucleus accumbens while the caudal part receives very few projections. It may be suggested that the rostral and middle part are the site of receiving informations and integrated by networks of nucleus before sending out the outflow to other areas of the brain (including globus pallidus) via the neurons in the caudal part.