9. Summary

The present study was designed to investigate the dissociable involvement of the striatal and hippocampal cholinergic systems in spatial localization.

Animals use extramaze cues (mainly visual and odor) in performing spatial tasks such as the radial arm maze (Zoladek & Robert, 1978). It has long been dominant that so-called cognitive map (O'Keefe & Nadel, 1978), which is assumed to be internally stored within organisms and helps animals locate themselves regardless of their body position and direction (also called as allocentric localization), mainly contributes to the spatial learning. Possible involvement of other factors such as egocentric localization, which is an ability to localize on the basis of animals' body position and direction, remains to be addressed. Yet, findings that normal animals showed both spatial (allocentric) and response (egocentric) strategies in a probe trial after acquiring T maze task (Thompson et al, 1980) and Morris water maze task (McDonald & White, 1994) strongly indicate that both egocentric and allocentric strategies are essential with regard to spatial localization. It is widely shown that the striatum and hippocampus are selectively involved in egocentric and allocentric localization, respectively. Therefore, it is presumable that both neural systems function simultaneously for efficient performance in spatial localization.

On the other hand, brain cholinergic systems have been studied for quite a long time as one of the major memory processing systems. Physostigmine, metabolite of ACh, impaired the one-way passive avoidance learning (Gammon & Thomas, 1980). Muscarinic receptor antagonist sco-

polamine impaired the retention of radial arm maze task (Hiraga & Iwasaki, 1984). Cholinergic activities show hypofunction correlating with retarded performance in learning and memory (Luine & Hearns, 1990). However, most of these findings focused on brain cholinergic systems as a whole and failed to show each cholinergic function that is region specific.

Therefore, in the present study, cholinergic systems in the striatum and hippocampus were investigated specifically with regard to spatially organized behavior.

Effects of intrastriatal and intrahippocampal injections of the cholinergic neurotoxin ethylcholine mustard aziridinium ion (AF64A) on performance of 8-arm radial maze task and two plus maze tasks were examined. In Exp. 1 and Exp. 2, a dose of AF64A to make a selective cholinergic lesion in the striatum and hippocampus were determined employing acetylcholinestrase staining and high performance liquid chromatography techniques. As a result, 1.8 nmol of AF64A resulted in selective decrease in ACh levels in the injected region (striatum and hippocampus). In Exp. 3, the retention of standard radial maze task was examined. Both striatal and hippocampal injections of AF64A impaired the retention of the radial maze task. The result suggests that both striatal and hippocampal cholinergic systems are involved in spatial localization. In Exp. 4 and 5, the retention and the acquisition of egocentric localization (EL) and allocentric localization (AL) tasks were examined. In EL task, an arm positioning in the same direction of a randomly selected start arm was baited throughout trials, whereas a baited arm was fixed throughout tri-

als regardless of the position of a start arm in AL task. The performance of the EL retention and EL acquisition was disrupted only by intrastriatal AF64A injection. In contrast, hippocampal AF64A injection selectively impaired the AL retention and AL acquisition. In addition, striatal lesioned animals showed better performance in the EL retention than in the EL acquisition. The hippocampal lesioned animals were impaired to the same degree in the AL retention and AL acquisition. In Exp. 6, effects of overtraining on the retention of the EL and AL tasks were examined. Overtrained striatal lesioned animals were better in their performance compared to the non-overtrained striatal lesioned animals in the EL task. Unlike the effect of overtraining on the EL retention in striatal lesioned animals, however, AL performance of hippocampal lesioned animals was not significantly affected by the overtraining.

The results demonstrate functional dissociation of the striatal and hippocampal cholinergic systems in EL and AL behavior and provided evidence that the striatal cholinergic system may be primarily involved in encoding process of EL learning and the hippocampal cholinergic system may be involved in both encoding and retrieval process of AL learning. Furthermore, it is indicated in the present study that the memory process impaired by the striatal cholinergic lesion may be spared by other brain systems based on the fact that the EL impairment of the striatal lesioned animals was milder in the EL retention than in the EL acquisition and overtraining had saving effect on the EL retention. In contrast, the memory process impaired by hippocampal cholinergic lesion may not be spared by other brain systems according to the fact that AL impairment of

the hippocampal lesioned animals were severe both in the retention and acquisition of the AL task to the same degree and overtraining had no saving effect on the AL retention. Yet, the striatal and hippocampal cholinergic systems appear to function simultaneously that each function of them is indispensable for an efficient performance in spatial localization.