The Role of Catecholamines in Retention Performance of a Partially Baited Radial Eight-Arm Maze for Rats

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Abstract

To assess the possible involvement of catecholaminergic neurotransmitters in maintenance of spatial cognition, the present work investigated the effects of dopaminergic and noradrenergic receptor antagonists on memory performance of rats in a partially baited radial eight-arm maze. Food-deprived rats were first trained to enter the arms baited with chocolate, and each subject was then randomly assigned to receive further training in either a place version or a cue version of the task. A specific pattern with four arms being baited was used throughout experimentation as the procedure for the place task; whereas four randomly chosen arms, each cued with a piece of sandpaper on the arm entrance, were baited from trial to trial as the procedure of the cue task. For drug evaluation, well-trained subjects were challenged with systemic injections of SCH23390, spiperone, haloperidol, prazosin, yohimbine, and propranolol. Regarding the place task, SCH23390, haloperidol, and propranolol, but not the other three drugs, significantly impaired behavioral performance by increasing the number of arm entries as well as the time to complete the task. The accuracy of performance as measured by the number of entries on the cue task was not significantly affected by any of these drugs tested. However, the times to complete the cue task were significantly increased with all drugs except yohimbine. These data show that blocking different catecholaminergic receptor subtypes produced distinct deficit patterns on the retention performance in a partially baited radial eight-arm maze. Evidently, both D1 and D2 dopamine receptors as well as β noradrenergic receptors are important in expression of spatial memory.

Key Words: dopamine, norepinephrine, place task, cue task, spatial memory, radial arm maze

Introduction

The development of the radial arm maze (RAM) task has provided a unique tool for assessing the neurobehavioral characteristics of memory processes based upon spatial cognition (21, 23). The cholinergic system has been found to be crucial for accurate RAM performance, as consistently supported by impairment of spatial memory induced by cholinergic blockade and lesions (for reviews, see 12 and 13). In addition to the cholinergic system, other neurotransmitter systems such as dopamine and norepinephrine are believed to be involved in maintenance of an accurate RAM performance. However, it is not clear what the exact role catecholamines play in RAM performance. In terms of previous studies examining drug effects on the performance of fully baited task of RAM, less work has been conducted with catecholaminergic drug treatments in comparison to that applied cholinergic agents.

More recently, different procedures using partially baited RAM have been developed to further examine the different processes involved in the RAM behavior such as spatial versus non-spatial memory. Packard and associates (25) compared win-shift and win-stay tasks in the RAM which required animal subjects to perform using spatial orientation and approaching a specific sensory cue, respectively. Using lesioning methods, they reported a double dissociation of mnemonic functions of the hip-

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pocampus and the caudate nucleus on these two tasks. Further evidence was provided by the post-training injection of low doses of dopamine agonists which enhanced memory in both the win-stay and win-shift tasks (32). Regarding spatial behavior, these data support theories of a dual-memory system that engages different neural systems (5, 11, 20, 22). It is thought that identifying the potential neural substrates or neurotransmitters related to the dual-memory system will assist in revealing the differential mechanisms of spatial memory. Accordingly, it was interesting to deal with this issue by evaluating the effects of distinct drugs with specific neuropharmacological characteristics on different tasks in the RAM. Two partially baited procedures in the RAM, the place and cue tasks, are believed to reflect spatial versus non-spatial memory. Both tasks require the subject to enter arms with bait and avoid entering arms with no bait or those never baited. Correct performance in the place task requires the use of distal, spatial, and extra-maze cues, whereas proximal and intra-maze cues are important for correct performance in the cue task. Currently, evidence of neural substrates relevant to these two tasks has been derived from the few studies using hippocampal lesions (10). It is still not clear how neurotransmitters modulate these two tasks. The present study was designed to examine the effects of drugs which block different catecholaminergic receptor subtypes on the place and cue tasks. If differences exist in the effects among drugs on particular tasks, then the role of certain catecho-laminergic receptor subtypes on either spatial or non-spatial memory can possibly be clarified. The agents used in this work were SCH23390 (a selective dopamine D1 receptor antagonist), spiperone (a selective dopamine D2 receptor antagonist), haloperidol (a non-selective dopamine D2 receptor antagonist), prazosin (a noradrenergic $\alpha 1$ receptor antagonist), yohimbine (an noradrenergic $\alpha 2$ receptor antagonist), and propranolol (a noradrenergic β receptor antagonist). The dose range for each drug applied in the present work had a low potential to induce complete akinesia or catalepsy, as referenced by previous work from this laboratory and others (2, 6, 7, 14, 15, 16, 19, 26).

Materials and Methods

Subjects

The subjects consisted of male Wistar rats, averaging approximately 250 g in body weight upon receipt. All rats were purchased from the Breeding Center of Experimental Animals at National Taiwan University Hospital, Taipei, Taiwan. They were allowed to adjust to their new environment, with access to food and water *ad libitum* for 10 days following arrival. For food deprivation, the rats were fed approximately 18 g of laboratory diet in their home cages no sooner than 30 min after the end of each daily experimental session. The subjects were thus maintained at 85% of their free-feeding weights throughout the experiment. Tap water was continuously available in each home cage. Training and/or test sessions were administered at the same time period during the light portion of the vivarium's 12/12-h light-dark cycle. The temperature of the colony was maintained at 23 ± 1 °C. Treatment of rats complied in all respects with the Chinese Psychological Association's ethical standards for the use of animals in research (4).

Apparatus

An eight-arm radial maze made of Plexiglas was used for training and testing. Each arm (61 cm L, 8 cm W, 15 cm H) extended from an octagonally shaped central platform (30 cm in diameter). A hole at the end of each arm served as a food well. The maze was elevated 80 cm from the floor. With the window blacked out, the maze room was illuminated by two 40-W fluorescent tubes positioned 270 cm above the center of the maze. Objects in the maze room such as a door, an air-conditioner, and black paperboard cut in different shapes and pasted on the wall served as extra-maze cues.

Drug Treatments

SCH23390 HCl, spiperone HCl, prazosin HCl, and yohimbine HCl were purchased from Research Biochemical Incorporate, while haloperidol and propranolol HCl were obtained from Sigma Chemical Company. SCH23390 HCl, spiperone HCl, propranolol HCl, and yohimbine HCl were dissolved with 0.9% saline. Haloperidol was dissolved in 0.9% saline with tiny drops of lactate. The solution was then adjusted to pH=3.5 with NaOH. Prazosin HCl was mixed with Tween 80 before being dissolved in warm saline. All drugs were injected via an IP route in a constant volume of 1 ml/kg of body weight. SCH23390 (0.05 and 0.10 mg/kg), spiperone (0.05 and 0.10 mg/kg), haloperidol (0.08 and 0.16 mg/kg), and propranolol (10 and 20 mg/kg) were administered 1 h before the commencement of a behavioral session, while prazosin (0.5 and 5.0 mg/kg) and yohimbine (0.5 and 5.0 mg/kg) were given 30 min before the beginning of a behavioral session.

Procedures

After initial acclimation to the colony room, there were two daily sessions of 5 min each in which

the rat was placed on the maze without bait in the arms. The subject was then trained to run down a single arm to obtain a piece of chocolate as the bait. Subsequently, rats were randomly assigned to learn either the place task or the cue task. The inside of the maze was wiped down with a clean towel between trials. For the place task, all eight arms of the maze were accessible but only four were baited. Each unit of bait consisted of a piece of chocolate (Meiji) weighing approximately 375 mg. The four baited arms were randomly selected. No more than two of the baited arms were directly across the central platform from each other or adjacent to one another. A unique combination of four baited arms was used for each rat throughout the experiment. At the beginning of the trial, an individual rat was placed within a transparent Plexiglas ring at the center of the maze. This ring was slightly lifted by hand about 5 sec after the rat had been placed in the maze; at the same time, a digital timer was started. All eight arms were open and were available for the rat to enter. Arm entry was counted when the entire body of the rat passed the line, which indicated where that particular arm of the maze attached to the central platform. The trial ended when the subject had retrieved all four pieces of bait, or when 10 min had elapsed. The initial entry into a baited arm was considered a correct choice. Entry into a previously visited arm or entry into a never-baited arm was considered an error. Thus, a well-trained subject normally completed a trial of the place task by visiting the four baited arms in the first four entries. One training trial was given per day, and the baseline was judged as the rat requiring five entries or less to complete the trial across three consecutive daily sessions. The time to complete the trial was recorded.

Regarding the cue task, four of the eight arms were baited as described in the preceding paragraph. However, a piece of sandpaper (CW100; 28 cm L, 7.5 cm W) was attached to the floor of the four baited arms to serve as a cue. The sandpaper was solidly placed 2 cm from the central platform across the mouth of the selected arm. The baited arms were randomly selected in each trial and were altered from trial to trial. The dependent variable and the acquisition criterion were similar to those for the place task.

Following 3 days of baseline, behavioral probe tests were conducted to certify that the current place and cue tasks required different types of information for correct performance. The probe tests for the place task applied to a group of 10 rats included rotating the maze and providing a mask of extra-maze cues. Manipulation in the former probe was achieved merely by rotating the maze 90°, while manipulation of the latter consisted of using pieces of white cloth to mask all the extra-maze cues. The aforementioned probe tests for the cue task were applied to a group of 13 rats. In addition, another probe utilizing the removal of cues was conducted specifically for the cue task. This probe was manipulated by removing all four pieces of sandpaper from the maze on the test day. Except for the specific probe procedure, the general maze procedures remained the same as those used for conducting either task in the training session.

Two separate groups of rats were trained to perform the place and cue tasks before pharmacological challenges. For either task, drug treatments were repeatedly conducted when a rat reached the criterion performance. A vehicle control was always administered in the session just prior to the drug treatment with a specific dose. There were five or more separate sessions for these vehicle/drug injections.

Statistical Analyses

A dependent *t*-test was conducted to evaluate the effects of behavioral probes and drug administration. Statistical significance was determined by an α value of 0.05 (two-tailed). Under the higher dose treatment, missing data appeared in some drug conditions when a subject did not fully complete the test trial. In other words, statistical analyses were performed only on data from subjects sufficiently motorically intact to complete the task within 10 min.

Results

The results of behavioral probes on the place and cue tasks are shown in Table 1. These data were collected over five daily sessions including three baseline days immediately before the probe, the probe testing day, and then 1 day of retraining. For the mask or rotation probe, performance on the place task over three baseline sessions was fairly stable ($P > 0.05$). As compared to the last day of the baseline, the mask manipulation significantly impaired the performance by increasing the number of entries, $t(9) = 6.532$, and the time to complete the task, $t(9) = 6.027$, (both $P < 0.001$). In contrast to the mask, the rotation probe did not significantly affect the performance of the place task. Regarding the cue task, no significant changes in the number of entries were observed when the mask or rotation was applied ($P > 0.05$). However, the time to complete the task significantly increased with the mask and rotation probes, $t(12) = 2.419$, $P < 0.05$, and $t(12) = 3.197$, $P < 0.01$, respectively. The probe with cue removal significantly disrupted the performance on the cue task by increasing the number of entries, $t(12) = 6.134$, and the time to complete the task, $t(12) = 6.363$ (both $P < 0.001$). For either task, the subject

Table 1. The Effects of Behavioral Probes on the Place (n=10) and Cue (n=13) Tasks.

Place task	Baseline 1	Baseline 2	Baseline 3	Mask	Retraining
number of entries	4.33±0.24	4.33±0.24	4.00±0.00	9.33±0.82**	4.33±0.17
time of complete task	36.78±5.65	36.22±5.68	29.67±3.31	93.00±10.64**	36.00±4.04
Place task	Baseline 1	Baseline 2	Baseline 3	Rotation	Retraining
number of entries	4.70±0.15	4.60±0.22	4.50±0.22	4.40±0.16	4.40±0.16
time to complete task	48.40±4.50	42.00±4.19	43.80±4.29	43.30±4.06	39.00±5.05
Cue task	Baseline 1	Baseline 2	Baseline 3	Mask	Retraining
number of entries	4.69±0.21	4.39±0.14	4.46±0.22	4.54±0.22	4.62±0.21
time to complete task	32.15±2.41	35.39±2.62	33.62±3.44	47.85±6.02*	36.00±3.67
Cue task	Baseline 1	Baseline 2	Baseline 3	Rotation	Retraining
number of entries	4.46±0.18	4.54±0.14	4.46±0.22	4.54±0.22	4.77±0.20
time to complete task	35.00±2.86	34.39±3.57	32.31±3.60	42.08±3.63**	30.39±3.35
Cue task	Baseline 1	Baseline 2	Baseline 3	Removal of cue	Retraining
number of entries	4.77±0.17	4.46±0.14	4.15±0.10	10.69±1.03**	4.46±0.22
time to complete task	18.77±1.01	18.23±1.56	16.15±1.04	84.00±10.78**	23.31±2.67

Data represent mean ± S.E.M. The unit for the time to complete task is second. *$P < 0.05$, **$P < 0.01$ significant difference from Baseline 3

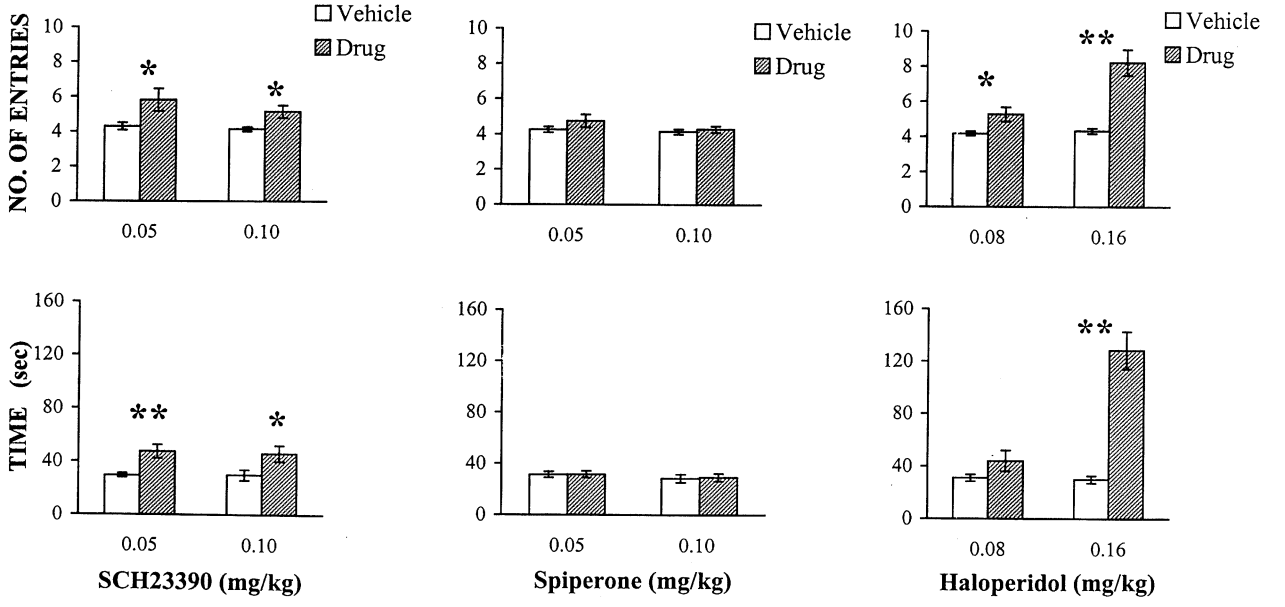

Fig. 1. Effects of dopaminergic receptor antagonists (SCH23390, spiperone, and haloperidol) on the place task as revealed by the mean number of entries (top) and the average time to complete the task (bottom). Each bar is expressed as the mean ± S.E.M. * $P < 0.05$, ** $P < 0.01$ indicate a significant difference as compared with the corresponding vehicle control.

resumed a good performance on the retraining day as compared to the baseline level.

Drug effects on the place task are presented in Figs. 1 and 2. Regarding the dopaminergic antagonists, the effects of SCH23390, spiperone, and haloperidol are presented in Fig. 1. The numbers of entries significantly increased with both doses of SCH23390, $t(9) = 2.5$ for 0.05 mg/kg and $t(7) = 2.37$ for 0.10 mg/kg (both $P < 0.05$). SCH23390 also significantly increased the time to complete the task, $t(9) = 3.4$, $P < 0.01$, for 0.05 mg/kg and $t(7) = 2.38$, $P < 0.05$, for 0.10 mg/kg. Neither dose of spiperone significantly affected the dependent variables measured for the place task. As shown in the right two panels of Fig. 1, both doses of haloperidol significantly increased the number of entries, $t(10) = 2.39$, $P < 0.05$, for 0.08

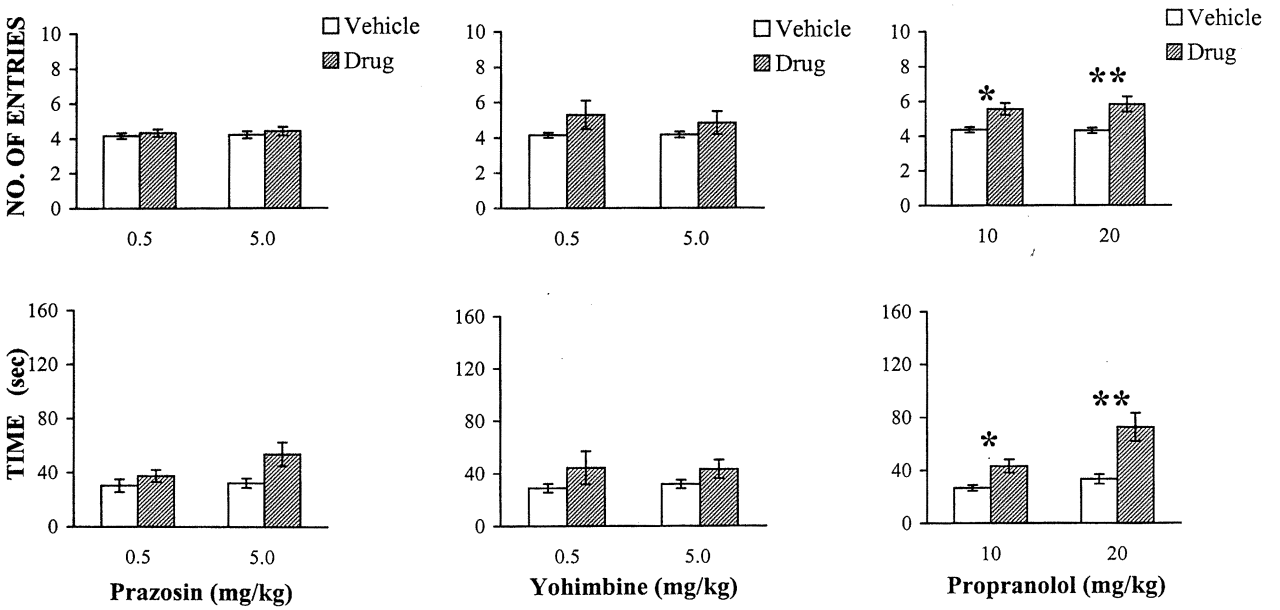

Fig. 2. Effects of noradrenergic receptor antagonists (prazosin, yohimbine, and propranolol) on the place task as revealed by the mean number of entries (top) and the average time to complete the task (bottom). Each bar is expressed as the mean ± S.E.M. * $P < 0.05$, ** $P < 0.01$ indicate a significant difference as compared with the vehicle control.

mg/kg and $t(8) = 5.75$, $P < 0.01$, for 0.16 mg/kg. Also, the time to complete the task significantly increased with the high dose of haloperidol, $t(8) = 6.41$, $P < 0.01$, but not by the low dose (0.08 mg/kg). The effects of the three noradrenergic antagonists on the place task are illustrated in Fig. 2. Neither prazosin nor yohimbine disrupted the rat's performance on the place task ($P > 0.05$). As shown in the right two panels of Fig. 2, the number of entries significantly increased with either dose of propranolol, $t(10) = 2.59$, $P < 0.05$, for 10 mg/kg and $t(9) = 3.31$, $P < 0.01$, for 20 mg/kg. The time to complete the task significantly increased with either dose of propranolol, $t(10) = 3.02$ for 10 mg/kg and $t(9) = 3.8$ for 20 mg/kg (both $P < 0.05$).

In terms of dose-effect evaluation for the place task, a repeated *t*-test was conducted to directly compare the effects of low and high doses for each drug. For the number of entries, only a significant difference between doses was revealed for haloperidol, $t(8) = 2.811$, $P < 0.05$. For the time to complete task, the between-dose difference was significantly confirmed for haloperidol, $t(8) = 4.923$, $P < 0.01$; for prazosin, $t(4) = 2.885$, $P < 0.05$; and for propranolol, $t(8) = 3.546$, $P < 0.01$.

Figures 3 and 4, respectively, present the effects of dopaminergic and noradrenergic antagonists on the cue task. In Fig. 3, neither dose of SCH23390 significantly affected the number of entries. However, the high dose, but not the low dose, of SCH23390 significantly increased the time to complete the cue task, $t(9) = 0.37$, $P < 0.01$. While neither dose of spiperone significantly affected the number of entries of the cue task, spiperone significantly affected the time to complete the task at either dose, $t(8) = 2.52$ for 0.05 mg/kg and $t(8) = 2.88$ for 0.10 mg/kg (both $P < 0.05$). As shown in the two panels on the right of Fig. 3, haloperidol did not significantly change the number of entries on the cue task at the doses used. However, the time to complete the cue task was significantly increased by haloperidol at a dose of 0.16 mg/kg, $t(12) = 2.93$, $P < 0.05$. In Fig. 4, neither dose of prazosin significantly affected the number of entries on the cue task. The high dose, but not the low dose, of prazosin significantly increased the time to complete the cue task, $t(7) = 4.45$, $P < 0.01$. In the middle two panels of Fig. 4, yohimbine did not significantly affect the performance of the cue task on the two measured variables. As shown in the two panels on the right of Fig. 4, neither dose of propranolol significantly changed the number of entries on the cue task. In contrast, the times to complete the cue task were significantly increased by propranolol at the two doses tested, $t(12) = 2.19$, $P < 0.05$, for 10 mg/kg and $t(12) = 3.7$, $P < 0.01$, for 20 mg/kg.

In terms of dose-effect evaluation for the cue task, a repeated *t*-test was conducted to directly compare the effects of low and high doses for each drug. For the number of entries, none of the six drugs produced a significant difference between doses ($P > 0.05$). For the time to complete task, the between-dose difference was significantly confirmed for

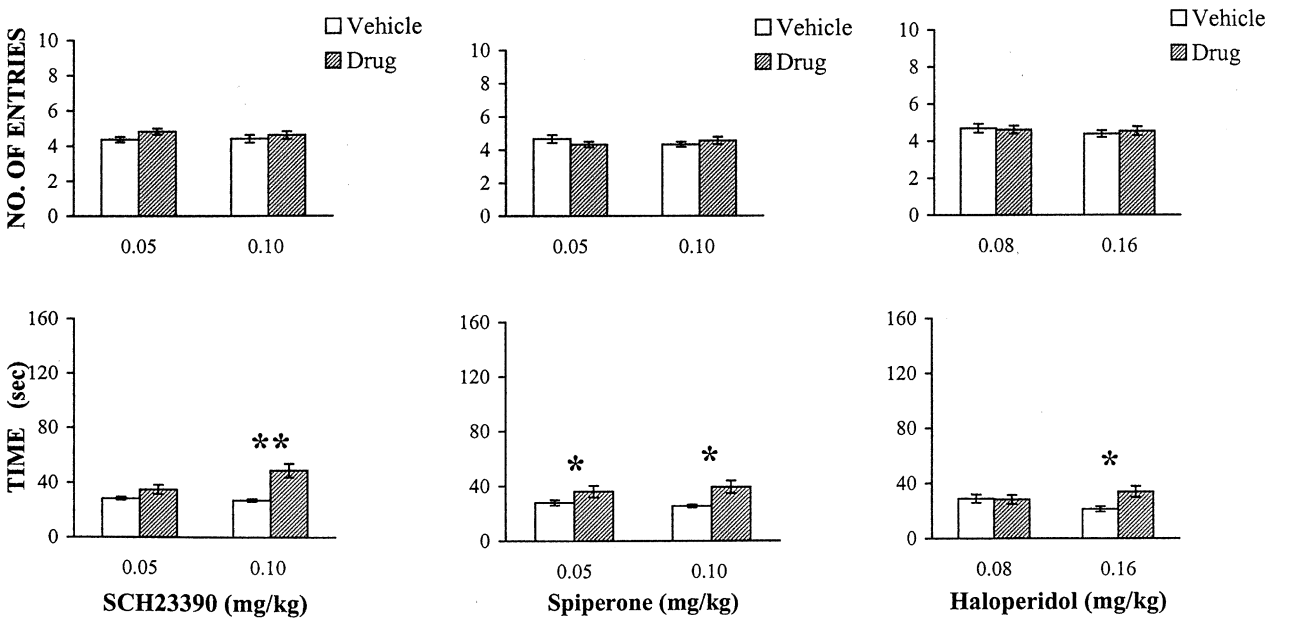

Fig. 3. Effects of dopaminergic receptor antagonists (SCH23390, spiperone, and haloperidol) on the cue task as revealed by the mean number of entries (top) and the average time to complete the task (bottom). Each bar is expressed as the mean ± S.E.M. * $P < 0.05$, ** $P < 0.01$ indicate a significant difference as compared with the corresponding vehicle control.

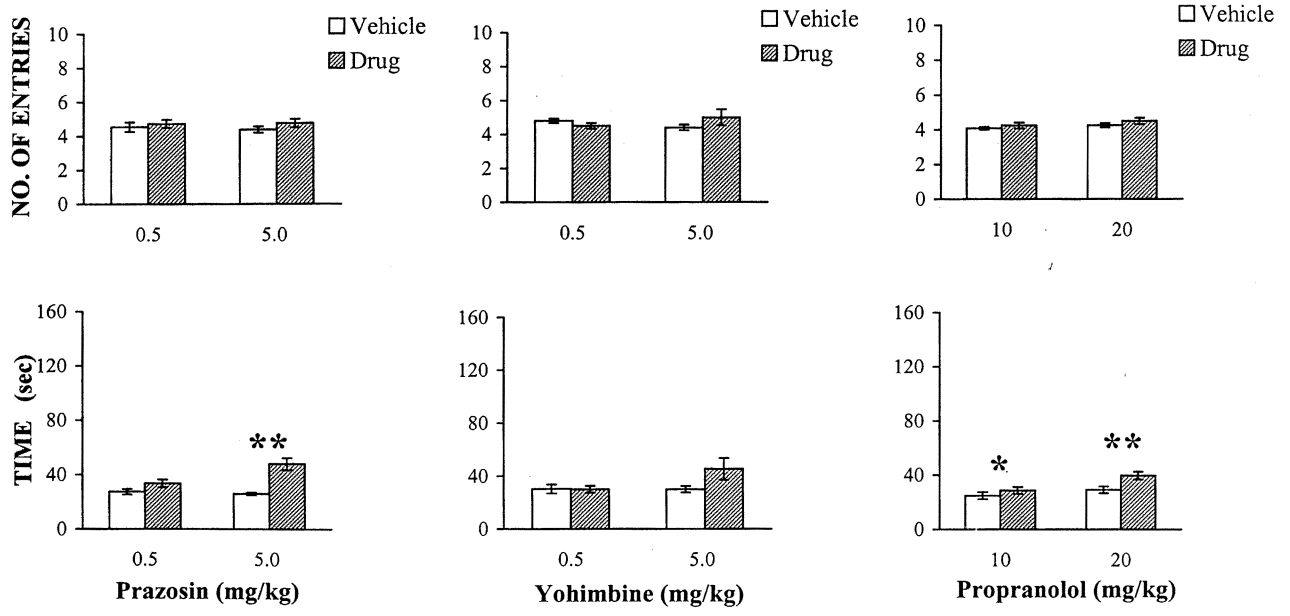

Fig. 4. Effects of noradrenergic receptor antagonists (prazosin, yohimbine, and propranolol) on the cue task as revealed by the mean number of entries (top) and the average time to complete the task (bottom). Each bar is expressed as the mean ± S.E.M. * $P < 0.05$, ** $P < 0.01$ indicate a significant difference as compared with the vehicle control.

SCH23390, $t(9) = 3.211$, $P < 0.05$; haloperidol, $t(8) = 3.411$, $P < 0.01$; for prazosin, $t(7) = 3.67$, $P < 0.01$; and for propranolol, $t(12) = 5.392$, $P < 0.01$.

Discussion

By using two distinct procedures in a partially baited RAM, the present study demonstrates that drugs blocking specific receptor subtypes of catecholamine systems differentially affected the performances on the place and cue tasks. Regarding the place task, SCH23390, haloperidol, and propranolol significantly impaired this spatial orientation behavior by increasing the number of arm

entries and the time to complete the task. No such impairment on the place task was observed for spiperone, prazosin, or yohimbine. In contrast to drug-induced impairment on the place task, the accurate performance on the cue task as measured by the number of entries was not significantly affected by any of the drugs tested in the present study. However, the times to complete the cue task significantly increased with all drugs except yohimbine.

From the probe tests, two sets of information (i.e., spatial versus non-spatial) appear to be distinctly involved in behavioral processing for the place and cue tasks adopted in the present study. On the place task, the mask manipulation rather than rotation significantly disrupted a subject's performance. These data clearly indicate that the correct performance on the place task relied upon extra-maze cues processed in a spatial manner. Neither the mask nor the rotation test significantly affected the accurate performance on the cue task. Although the time to complete the cue task significantly increased with either test, the magnitude of that increase using the mask or rotation on the cue task was less apparent than that using the mask on the place task. The most profound disruption of performance on the cue task, as compared to three probe tests, was observed when the sandpaper cues were removed from the maze. This then suggests that the current cue task be related to a non-spatial process mainly by adopting the sandpaper as an intra-maze cue to guide the correct response. These differential characteristics on the place and cue tasks revealed from behavioral probing support the notion that *locale* and *taxon* systems exist for guiding different types of spatial behaviors (20). Moreover, it is now believed that different neural systems are involved in behavioral performances for place and cue tasks of the RAM. The hippocampus is important for processing spatial information on the place task, the argument for which has been supported by the sole impairment on the place task of RAM observed from direct hippocampal lesions in the rat (9). Convergent evidence from the Morris water maze showed that deficits in place navigation rather than the cue-related response appeared in rats with selective lesions in the hippocampus (18, 30, 31). Different roles for the hippocampus and the caudate nucleus involved in place- and cue-oriented responses were inferred from a recent study employing a simple cross maze. Packard and McGaugh (24) reported that behavioral performances of place (spatial-related) and response (stimulus/response-associated) learning were suppressed after lidocaine-induced inactivation of the hippocampus and caudate nucleus, respectively.

Each drug used in the present study possesses selectivity to antagonize a particular subtype of catecholaminergic receptor. That accurate performance on the place task was impaired by SCH23390, haloperidol, and propranolol suggests that dopamine D1 and D2 as well as noradrenergic β receptors are important for the retention of the place task. In contrast, no significant impairment on the place task with spiperone, prazosin, or yohimbine indicates that dopamine D2 receptors alone and noradrenergic α receptors are not critical for the expression of this type of spatial behavior. Although both D1 and D2 receptors were indicated as being involved in the performance on the place task, the D1 subtype may be more critically important than the D2 subtype. This is simply because the profound drug effects on the place task were revealed with SCH23390 rather than spiperone. Also, this notion is supported by comparing the different capabilities of spiperone and haloperidol in blocking D2 receptors. While spiperone is a selective blocker of D2 receptors, haloperidol as a mixed D1/D2 receptor antagonist potently blocks D2 receptors and has some effects in blocking D1 receptors as well (29). Thus, behavioral deficits on the place task induced by haloperidol could be via the drug blocking dopaminergic receptors in both the D1 and D2 subtypes. Different degrees of occupancy might be considered as well. Although the possibility that the lack of effects of spiperone could be due to inadequate doses applied in the present work cannot be completely excluded, one must consider that the same doses of this drug did affect the performance on the cue task to a certain extent.

That neither yohimbine nor prazosin altered the spatial performance on the place task indicates that the noradrenergic $\alpha 1$ or $\alpha 2$ subtype receptors are unlikely to be involved in the rat's performance on this task. In contrast to the lack of an effect of drugs blocking the noradrenergic α receptors, propranolol as a β blocker did impair performance on the place task. Although the noradrenergic neurotransmission system is known to be very important in the modulation of memory processes and storage based on inhibitory avoidance retention (for reviews, see 3, 17), only a few studies have collected data on revealing noradrenergic's role in spatial behavior. Systemic administration of propranolol alone did not affect retention in the water maze, whereas significant deficits were observed when propranolol was given in combination with scopolamine, a cholinergic antagonist (6). Such findings were also demonstrated on a fully baited RAM (19). Using place and cue tasks similar to those in the present work, adverse effects of an increased number of errors on either task were produced by pretreatment with propranolol at a dose of 5 mg/kg, but not 0.5 mg/kg (7). Concerning differences between the blockade of peripheral and central β receptors, Williams and associates (35) examined the systemic effects of sotalol and pro-

pranolol (2 mg/kg) given before a session on the amphetamine-induced retention improvement on the win-shift task of an eight-arm maze with an 18-h delay. Both sotalol and propranolol impaired the 4-OH amphetamine-induced facilitation, but not that of d-amphetamine. Behavioral effects produced by 4-OH amphetamine and d-amphetamine are assumed to be derived respectively from drug reactions on the peripheral and central catecholamine systems. That study also reported that memory retention produced by d-amphetamine was completely blocked by this propranolol treatment in combination with haloperidol at a non-effective dose when given alone. Together with the current data regarding the drug effects on the place task, it is thus suggested that noradrenergic β receptors are involved in spatial behavior on the RAM.

If the involvement of dopamine systems is critical for the maintenance of correct spatial behavior, then any drug or brain manipulation inducing dopaminergic dysfunction should disrupt the behavioral performance on either the RAM or the water maze. Data collected from previous work using the water maze are comparable to the present findings. Studies using neurotoxin 6-hydroxydopamine lesions have implicated the nigrostriatal dopamine pathway in the learning of spatial behavior in the Morris water maze (33). Systemic administration of modest doses (0.04 and 0.07 mg/kg) of haloperidol was demonstrated to impair the spatial version of the water maze performance using an invisible platform, but not the cue version with a visible platform (26). The same authors further reported similar results using a local infusion of haloperidol into the nucleus accumbens (27). These two tasks in the water maze can correspond to the current tasks on the partially baited RAM, and the results highlight that haloperidol affects neurobehavioral processing of spatial rather than non-spatial (or cue-related) information. Moreover, the other types of tasks on the partially baited RAM suggest that behavioral deficits induced by drugs are task-dependent. Haloperidol was reported to disrupt working memory in a delayed procedure on the RAM, for a task that is similar to the win-shift task requiring spatial information (2). However, chlorpromazine, a traditional antipsychotic drug also known as a non-selective dopamine receptor antagonist, did not affect the performance on a fully baited RAM (8). Reversible lesions on the nucleus accumbens produced by lidocaine were shown to impair the spatial win-shift, but not the cued win-stay, on the RAM (28). Combining these data with those collected from studies using other memory-related tasks, it has been argued that the role of dopamine D1 receptors in the brain (i.e., the prefrontal cortex) is essential for memory storage and retrieval (1, 34). Also with the apparent drug effects which appear for haloperidol and SCH23390 on the place task, it is likely that the deficits with haloperidol are mediated primarily by the D1 receptor blockade, with D2 receptors playing a more permissive role.

While SCH23390, haloperidol, and propranolol affected the accurate performance on the place task, these three agents did not impair the correct performance on the cue task. Although these three drugs did not increase the number of arm entries, the time to complete the task was significantly lengthened. These results show that subjects under these drug treatments exhibited slowed motoric movement on the cue task inside the maze, yet they were still able to make the correct arm entry. In comparison to the place task, the behavioral performance on the cue task was more resistant to these three antagonists. Two issues can be raised about these results. First, in order to judge how catecholamines are involved in learning and memory on the cue task, further study needs to examine the effects of these catecholaminergic antagonists on the acquisition, instead of the performance, of the cue task. Because the present work examined the effects of catecholaminergic antagonists on the performance phase of the cue task, it is possible that the drugs would influence the acquisition of the cue task when subjects were not as well-trained as those reported here. Second, differential effects of catecholaminergic antagonists on the place and cue tasks may be due to different degrees of effort demanded in the performance of these two tasks. To correctly perform the place task required more effort from cognitive processing to behavioral reactions than did the cue task. Thus, the mnemonic requirement is higher for the place task than for the cue task. It is possible that the performance of the place task with its higher mnemonic requirement would be more easily interrupted by dopamine receptor antagonists (i.e., SCH23390) than would the cue task.

In conclusion, this study presents two distinct tasks requiring utilization of spatial and non-spatial strategies on a partially baited eight-arm RAM. Current data from drug evaluation show that blocking different catecholaminergic receptor subtypes produced distinct deficit patterns on the memory performance in a partially baited radial eight-arm maze, for which the effectiveness was task-dependent. Evidently, both D1 and D2 dopamine receptors as well as β noradrenergic receptors are important in the expression of spatial memory.

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