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Differences in the Acquisition Process and the Effect of Scopolamine on Radial Maze Performance in Three Strains of Rats

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HIGASHIDA, A AND N OGAWA *Differences in the acquisition process and the effect of scopolamine on radial maze performance in three strains of rats* PHARMACOL BIOCHEM BEHAV 27(3) 483–489, 1987 —The acquisition process and the effect of scopolamine (SCOP) on the radial maze task were studied in 3 strains of male rats, Fischer 344 (F344), Sprague-Dawley (SD) and Wistar The pretraining level of locomotor activity was measured and performance was quantitatively and qualitatively evaluated The highest pretraining locomotor activity was observed in Wistar rats In this experiment, rats were allowed to select each arm successively The changes in the number of correct choices during the first eight selections, error choice in a trial and the total duration of a trial differed with the strain in the first 5 training sessions Acquisition curve for F344 rats gradually rose Wistar rats made many error choices However, during the final 5 sessions, only the total duration of a trial differed with the strain Wistar rats took the shortest time to finish a trial, but the number of sessions taken to acquire this task was the fewest with F344 rats, and the most with Wistar rats The effect of SCOP differed among strains in all the above 3 indexes Generally, the Wistar rat was the most affected by the injection of SCOP Moreover, the change of the choice accuracy and the spatial strategy by the administration of SCOP were investigated SD and Wistar rats showed a dose-dependent decrease in choice accuracy in the earlier selection The spatial strategy was changed in every strain by the injection of SCOP These findings do not support the previous finding that a high level of locomotor activity yields fast acquisition of this task or that Wistar rats are better in learning than SD, but indicates that SCOP affects not only the working memory but also the motivational factor

Strain difference Scopolamine Radial maze Spatial memory Spatial strategy Rats

THE radial maze task was initally devised for studying spatial memory in the rat [12] This task involves successive selection of a number of arms radiating from the center of the maze to obtain food as a reward The optimal strategy is to select each arm once and avoid re-entering an arm from which the reward had been removed during a previous choice [2] Therefore, the animal must memorize or remember each choice during a trial to perform accurately The information an animal memorizes or remembers is only available in a trial, and the animal should discard that information on the next or other trials Such a memory process should be involved in this maze solving Therefore, accurate performance is considered to be mediated by working memory [6,13]

Many reports have shown that the accurate performance in this task is profoundly impaired by the damage of the cholinergic nervous system such as IP injection of the antimuscarinic cholinergic agent scopolamine (SCOP) [3–5, 15, 18, 19], ICV administration of the presynaptic cholinergic neurotoxin AF64A [8,17] or hippocampal lesion [7,16]

The correct choices in the first eight selections [2,5], error choices in a trial [7], pattern of response [17] and choice accuracy [4] using an eight-arm radial maze have been reported

On the other hand, in spite of many reports of the effect of SCOP on this maze performance, the differences in the acquisition or the effect of SCOP in different strains of rats has not been reported However, a comparative study on two inbred strain of mice has been reported [1], and it suggested a significant correlation between locomotor activity and performance in this task

Moreover, it was previously reported that when rats were trained by a conditioned avoidance procedure reinforced by aversive electric stimuli, the highly active Wistar strain could learn faster than the less active Sprague-Dawley (SD) [9,11] Therefore, we examined the differences in the acquisition process and the effect of SCOP on this task in three strains of rats, Fischer 344 (F344), SD and Wistar

METHOD

Subjects

Ten experimentally naive male rats (10 weeks of age) of F344, SD and Wistar were used The animals were housed

TABLE 1
DRUG DESIGN

Strain	Order										
Fischer-F344	BL1	SA1	0 5	SA2	1 0	SA3	0 25	SA4	BL2		
Sprague-Dawley	BL1	SA1	0 5	SA2	1 0	SA3	0 25	SA4	0 125	SA5	BL2
Wistar	BL1	SA1	0 5	SA2	1 0	SA3	0 25	SA4	0 125	SA5	BL2

Values represent the dose of scopolamine (mg/kg)
BL—Baseline SA—Saline

individually with free access to food and water in an illumination controlled room (light period, 0700–1900, dark period, 1900–0700) The room temperature was kept at 25°C and the humidity was kept at 55% After adaptation to this room, their body weights were reduced by food deprivation and subsequently maintained at 80% of their initial values During this period rats fed a small quantity of sugar pellets in their home cage subsequently were utilized as reinforcers

Apparatus

Behavioral testing was conducted in an eight-arm radial maze made of wood, painted gray This maze was made according to [5] after slight modification It was elevated 50 cm above the floor, and consisted of an octagonal central platform (30 cm wide) surrounded by eight equally spaced radial arms (60 cm long × 12 cm wide) Small plastic cups painted black mounted at the end of each arm, were 1 0 cm deep and 2 0 cm in diameter At the entrance of each arm, a guillotine door, painted white on the platform side and painted black on the arm side, was set to control the start and finish of a trial The tests were carried out in a white painted sound-attenuated room lit by three 60 W tubes Several visually distinct cues (e g , desk, operating tables) were present in the room The maze was kept in the same place throughout the experiment

Procedure

Pretraining The rats were initially adapted to the maze Each rat was placed on the platform and 30 seconds later, all guillotine doors were raised and the rat was allowed to explore and eat the sugar pellets scattered in the arms and put in the cups at the end of each arm When the rats had entered all the arms and had eaten all the sugar pellets from the cups within 10 minutes or less, formal training was started This procedure was performed once a day, and the number of entries into the arms within a trial and the number of sessions until the rat entered all arms within 10 minutes, were recorded

Formal training procedure Each rat performed one session a day At the start of each session, a sugar pellet (20 mg) was placed in all cups Each rat was placed on the platform, and 30 seconds later all guillotine doors were raised permitting access to any of the arms When the rat had entered all arms and had looked into all cups or 10 minutes had elapsed, all guillotine doors were lowered and the rat was taken off the maze and brought back to its home cage The rat chose and entered each arm spontaneously, and when it entered an arm which it had not entered yet, and looked into the cup, this selection was defined as correct choice, while the rat that re-entered an arm which it had already selected and looked into the cup without turning back, was defined to have made an error choice

When a rat made correct choices seven successive times in the first eight selections in a trial, that rat was considered to have learned the task when it maintained this performance for five sessions successively [5]

Recording method The order of the arms the rat entered and looked into the cup, and the total time elapsed before the rat had entered all arms and looked into all cups, were recorded The rats ate the pellets without fail when they looked into the cups in the formal training session, but in a few cases they did not eat the pellets when they had been injected a high dose of SCOP, the choices were recorded as mentioned above

Drug treatment Scopolamine hydrobromide (Wako Pure Chemical Industries) was dissolved in physiological saline The animals that were considered to have acquired the task, were injected various doses of this solution IP 30 minutes prior to testing according to Table 1 To eliminate possible carry-over effects of SCOP, the control sessions were inserted among every SCOP session In the control sessions, the animals were injected saline in the same way

Statistical Analysis Overall treatment effects were assessed by analysis of variance (ANOVA) procedures Appropriate pair-wise comparisons were performed with a paired t-test Acceptable statistical significance was established as $p<0$ 05

RESULTS

Pretraining

Pretraining was begun when the animal's body weights became 80% of its initial value, and it ate sugar pellets in its home cage The number of sessions until a rat entered all arms and the number of animals which entered all arms did not differ significantly with the strain, F344, SD or Wistar On the other hand, as at least three sessions were required until each rat entered all arms, the numbers entered into the arms in the first three sessions were analyzed by the two-way [Strain(3) × session(3)] ANOVA Analysis of the data revealed a significant difference with the strain, $F(2,81)=6$ 66, $p<0$ 01 Moreover, a significant difference was observed between session, $F(2,81)=15$ 67, $p<0$ 01, but the interaction effect between strain and session was not significant, $F(4,81)<1$ 0 The Wistar strain entered the arms the most frequently

Formal Training

The formal training was started as soon as the animal had been able to enter all arms As some animals showed criteria performances on the first session and maintained these per-

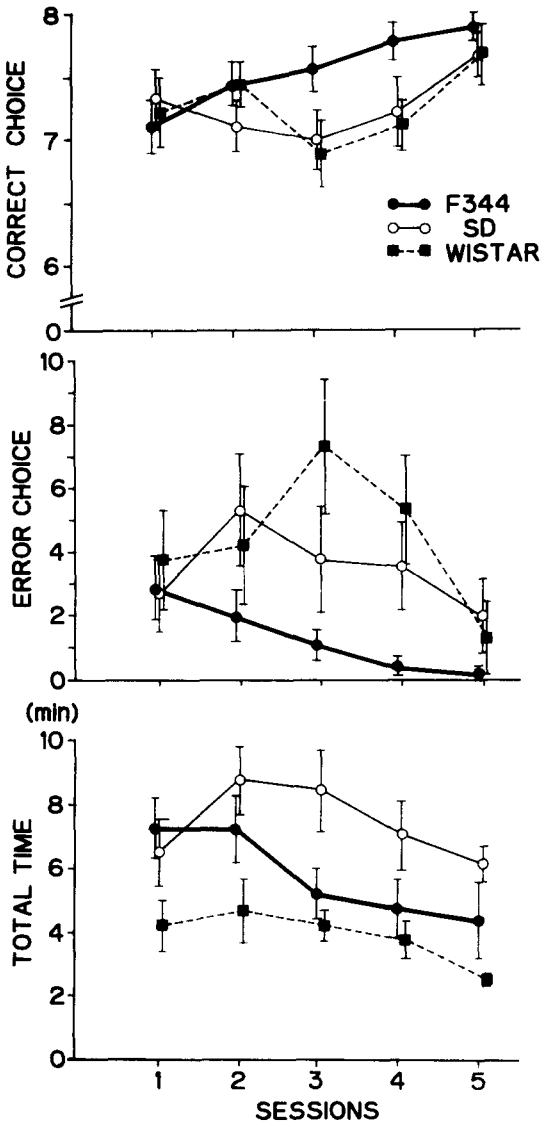

FIG 1 Correct choice in the first eight selections, error choice in a trial and total duration of a trial for the first 5 sessions in each strain Each value represents the mean±SEM

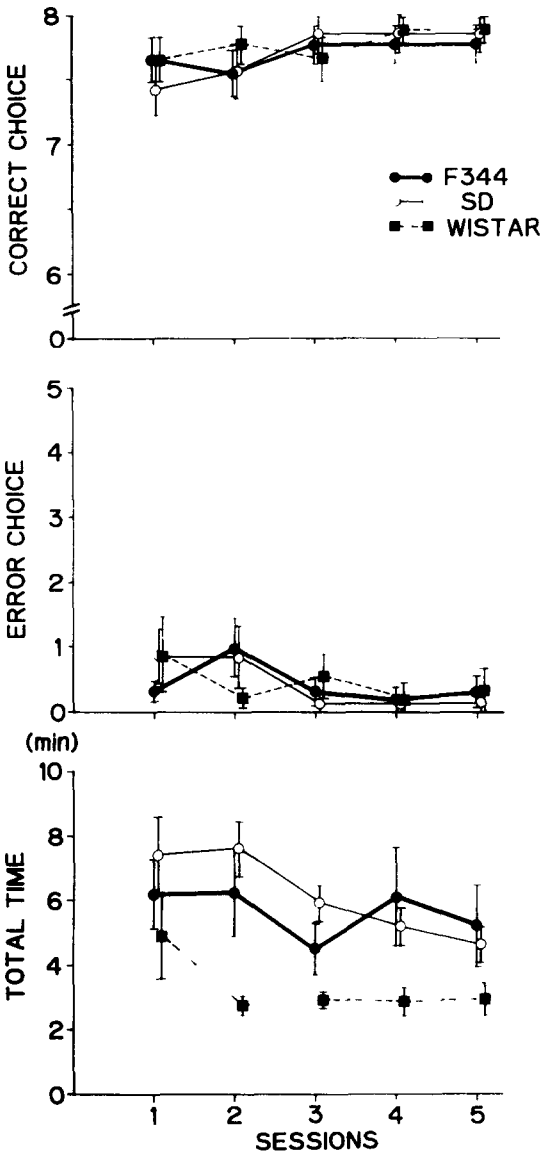

FIG 2 Correct choice in the first eight selections, error choice in a trial and total duration of a trial for the final 5 sessions in each strain Each value represents the mean±SEM

formances for five sessions successively, the acquisition process was analysed in the first five sessions

However, one rat each of the F344 and SD strains did not run in the maze in the formal training sessions These animals were excluded from all analyses One Wistar strain rat caught cold in the initial stage of training This animal was excluded from the analysis in the training sessions, but as this rat could run stably in the final stage of training, it was used in the drug treatment session The training period was 12 sessions at most, but two animals in SD strain could not acquire the task during this period One of them acquired the task in the 13th session These animals were used in the evaluation of the first five training sessions, but were then excluded In total, nine animals of each strain were used in the evaluation of the first five sessions, and nine F344 rats, nine Wistar rats and seven SD rats were used in the evaluation of the final five sessions

Figure 1 shows the changes in correct choices in the first eight selections, the changes in error choices in a trial and the changes in the total duration of a trial, respectively A two-way [Strain(3) × session(5)] ANOVA for each index was carried out In the correct choice, there were significant differences with the strain, $F(2,120)=3\ 15$, $p<0\ 05$, and session, $F(4,120)=3\ 56$, $p<0\ 01$, but the interaction between strain and session was not significant, $F(8,120)=1\ 03$, $p>0\ 05$ In the error choice, there was a significant difference with the strain, $F(2,120)=6\ 91$, $p<0\ 01$, but not with the session, $F(4,120)=2\ 17$, $p>0\ 05$, or the interaction between strain and session, $F(8,120)=1\ 05$, $p>0\ 05$ In the total duration, significant differences were revealed with the strain, $F(2,120)=18\ 50$, $p<0\ 001$, and session, $F(4,120)=3\ 24$, $p<0\ 05$, but the interaction between strain and session was not significant, $F(8,120)<1\ 0$ According to Fig 1, F344 made gradually more correct choices, and gradually fewer

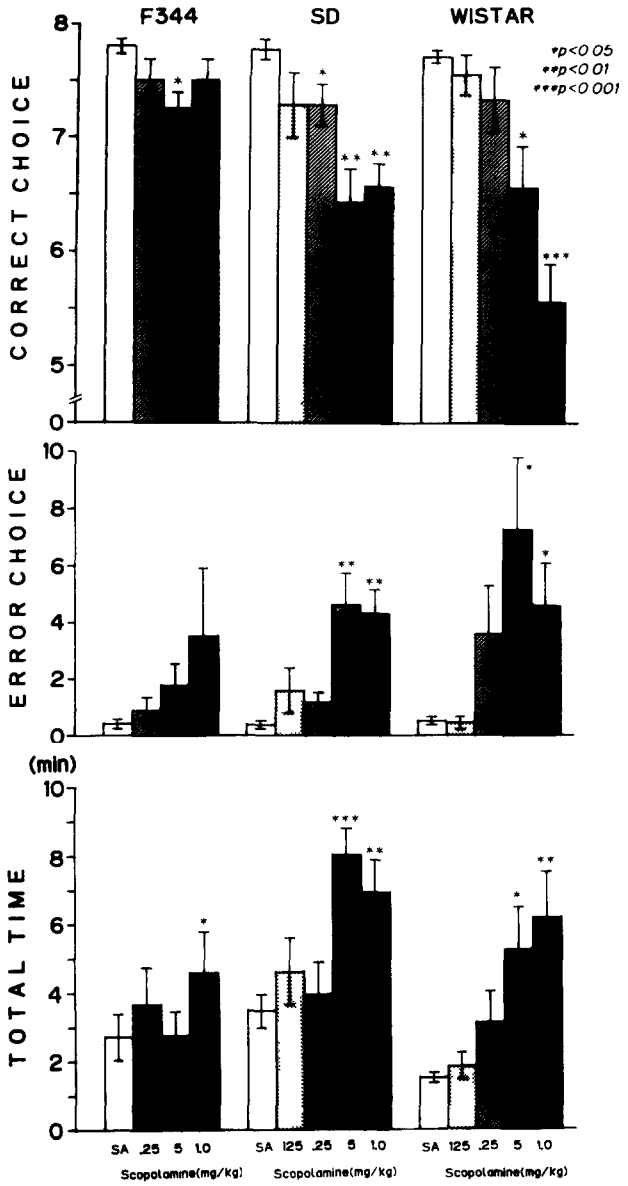

FIG 3 Correct choice in the first eight selections, error choice in a trial and total duration of a trial at various doses of scopolamine in each strain Each value represents the mean±SEM SA—Saline *=$p<0$ 05, **=$p<0$ 01, ***=$p<0$ 001, compared with SA analyzed by paired t-test

TABLE 2

ONE-WAY ANALYSIS OF VARIANCE IN SCOPOLAMINE INJECTED RATS

Fischer-344	
Correct Choice	F(4,67)=3 71†
Error Choice	F(4,67)=3 02*
Total Time	F(4,67)=0 95 N S
Sprague-Dawley	
Correct Choice	F(5,71)=12 47‡
Error Choice	F(5,71)=17 43‡
Total Time	F(5,71)=8 11‡
Wistar	
Correct Choice	F(5,93)=21 79‡
Error Choice	F(5,93)=9 64‡
Total Time	F(5 93)=13 26‡

Degrees of freedom represented in parentheses
Each value represents F-value
N S —not significant, *$p<0$ 05, †$p<0$ 01, ‡$p<0$ 001

TABLE 3

TWO-WAY ANALYSIS OF VARIANCE IN SCOPOLAMINE INJECTED RATS

Strain Difference	
Correct Choice	F(2,172)=15 86†
Error Choice	F(2,172)=6 51†
Total Time	F(2,172)=8 94†
Treatment (scopolamine injection)	
Correct Choice	F(3,172)=27 33†
Error Choice	F(3,172)=13 25†
Total Time	F(3,172)=12 74†
Interaction	
Correct Choice	F(6,172)=5 76†
Error Choice	F(6,172)=1 78 N S
Total Time	F(6,172)=2 66*

Degrees of freedom represented in parentheses
Each value represents F-value
N S —not significant, *$p<0$ 05, †$p<0$ 01

error choices session by session The error choice increased in the order of Wistar, SD and F344 The total duration of a trial increased in the order of SD, F344 and Wistar

The acquisition process was next analyzed for the final five sessions In these sessions, all animals maintained the criteria performances successively Figure 2 shows the changes in correct choices in the first eight selections, the changes in error choices in a trial and the changes in the total duration in a trial, respectively Two-way [Strain(3) × session(5)] ANOVA for each index was carried out similarly for the first five sessions In the correct choice, no significant differences were observed with any factors, strain, F(2,110)<1 0, session, F(4,110)=1 69, $p>0$ 05, or the interaction between strain and session, F(8,110)<1 0 Similarly, in the error choice, no significant difference was observed with any factor, strain, F(2,110)<1 0, session, F(4,110)=1 74, $p>0$ 05 or the interaction between strain and session, F(8,110)<1 0 However in the total duration of the trial, there was a significant difference with the strain, F(2,110)=12 98, $p<0$ 001, but not with the session, F(4,110)=2 14, $p>0$ 05 The interaction between strain and session was also not significant, F(8,110)<1 0 In the final five training sessions, i e , just prior to drug administration sessions, all strains displayed stable performance, but the strain difference was very clear in the total duration of a trial, especially the duration was the shortest for the Wistar rats

The number of sessions required to acquire this task, was 6 78±1 75 (mean±SEM) for the F344 rats, 8 00±2 50 (mean±SEM) for the SD rats and 9 00±2 24 (mean±SEM) for Wistar rats Among them, a significant difference between F344 and Wistar was revealed by Student's t-test

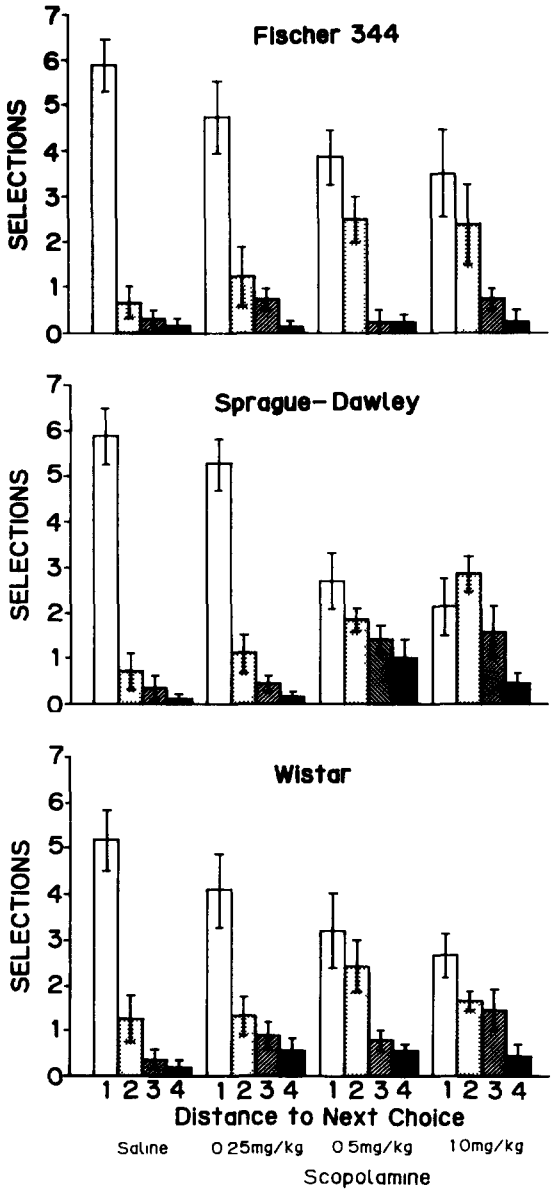

FIG 4 The relative frequency of selecting arms various distances (clockwise or counter-clockwise) from the arm just exited at various doses scopolamine in each strain

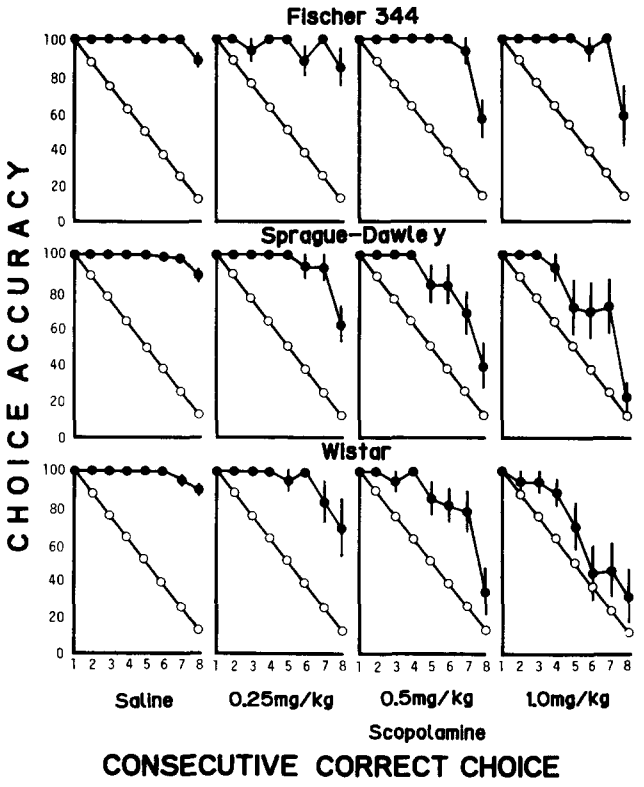

FIG 5 Accuracy of successive correct choice, i e , mean percent choices of new arms within a trial at various doses of scopolamine The diagonals represent the number of new arms which would be selected if the choice were a random selection Upper line represents Fischer 344 strain, middle line represents Sprague-Dawley and lower line represents Wistar strain, respectively

($t=2$ 29, $p<0$ 05) The F344 rats acquired this task faster than the Wistar rats The SD rat acquired this task in 13th sessions and was included in this analysis

Drug Treatment

Drug administration was started as soon as each animal had acquired the task One F344 and one Wistar rat would not run in the maze even on the saline sessions These animals were discarded In total, eight F344 rats, seven SD rats and nine Wistar rats were used in the evaluation of the effect of drug administration Figure 3 shows the effects of various doses of SCOP on the correct choice, on the error choice and on the total duration in a trial, respectively Table 2 shows the one-way ANOVA between drug and treatments (base line, saline, SCOP 0 125 mg/kg (only SD and Wistar), SCOP 0 25 mg/kg, SCOP 0 5 mg/kg and SCOP 1 0 mg/kg) in every index for each strain, respectively Only the effect of drug treatment on the total duration of a trial in F344 failed to reveal a significant difference Table 3 shows the two-way ANOVA between strain(3) and treatment(4, saline, SCOP 0 25 mg/kg, SCOP 0 5 mg/kg and SCOP 1 0 mg/kg) in every index Only the interaction between strain and treatment in the error choice failed to reveal significance Above all, the number of correct choices decreased significantly by SCOP administration in all strains, the effect being greater in the order of Wistar, SD and F344 rats The effect was dose-dependent for the Wistar rats The number of error choices increased significantly by SCOP administration in all three strains, the effect being greater in the order of Wistar, SD and F344 rats, but the tendency of increment did not differ between any strains The total duration of a trial differed with all strains, and was extended significantly in SD and Wistar but not in F344 rats The tendency of extention differed with the strain, and was dose-dependent in Wistar

Pattern of Response (Spatial Strategy)

Figure 4 shows the pattern of response for the first eight selections for F344, SD and Wistar rats, respectively Each horizontal line expresses the distances (clockwise or counter-clockwise) from the arm just exited, and each vertical line expresses the frequency of the selection In the saline

session, most of the rats in all the strains exhibited a marked preference for choosing the immediately adjacent arm, so the frequency was the highest for selecting the immediately adjacent arms However, this preference decreased dose-dependently with SCOP administration By contrast, the preference for choosing the arm of 90° direction increased dose-dependently

Choice Accuracy

Each arm was assigned a number from 1 to 8, and the arm number was recorded in the order the rat entered it For example, a rat selected arms *3, 4, 7, 2, 5,* 3, *6,* 4, 7, *8,* 2, 3, 5, *1* before the trial was finished The italicized number was the correct choice Until the fifth correct choice, this rat could select the correct arm in one choice The accuracy of choosing the correct arm was 100% until the fifth selection, but in selecting the sixth correct arm, this rat made one error and selected the correct arm at the second choice The accuracy of choosing the sixth correct arm for this rat is 50% Similarly, since in selecting the seventh correct arm this rat made two errors and could select the correct arm at the third choice, the accuracy of choosing the seventh correct arm is 33 3%, and the accuracy of choosing the eighth or final correct arm is 25% Thus, the accuracy of each correct choice in a trial was calculated for each animal Figure 5 shows the average choice accuracy for each correct arm at various doses of SCOP The choice accuracies, especially the final or eighth choice accuracy decreased dose-dependently for all strains Moreover, the SD and Wistar rats made more errors in the earlier selection dose-dependently with SCOP treatment In the F344 rats, the final choice accuracy decreased with SCOP treatment, but generally they were more resistant to the effect of SCOP than the SD or Wistar rats

DISCUSSION

In the pretraining session, using sugar pellets scattered in the maze, the Wistar rats showed the highest locomotor activity In the formal training sessions, the F344 rats, especially, made more correct choices, and fewer error choices session by session The Wistar rats had the shortest total duration of trial, but made many errors (Fig 1) During the final five sessions, all strains showed stable good performance, but the Wistar strain showed the shortest total duration of trial (Fig 2), i e , Wistar rats showed the highest locomotor activity

Activity has been reported to be correlated with performance on the same task in comparison with the two inbred strains of mice [1], but this correlation was not observed in this experiment Wistar rats showed the highest locomotor activity throughout the training session, but this strain required the most training sessions and also made the most errors The level of locomotor activity might not correlate with the performance of this task in these rat strains

On the other hand, Wistar rats have been reported to acquire the conditioned avoidance response faster than SD or F344 rats when aversive electric shock is used as an unconditioned stimulus [9,11], but this is also in discordance with the present observation Wistar rats made more errors in the first five sessions and required more number of training sessions than SD rats, but they could maintain good performance during the final five sessions Therefore, the working memory of the Wistar rats is not smaller than that of the F344 or SD rats Instead of an aversive unconditioned stimulus, a positive food reward was used in this experiment This difference of procedure produced a discrepancy between previous reports and the present results

During the SCOP administration schedule, all indexes, correct choices, error choices and total duration of the trial were altered significantly in the SD and Wistar rats The total duration of the trial was not altered in F344 rats (Table 2) However, significant differences among the strains were observed in all indexes (Table 3) Whereas no significant difference was detected with the interaction between strain and drug treatment in the error choice (Table 3) Therefore the increased error choice accompanied by the increase in the dosage of SCOP did not differ with the strain

In this experimental condition, rats were permitted to select each arm successively, i e , we did not interfere with the rat's choice between each selection Under this condition, many animals chose the arm immediately adjacent the arm just exited in the training session, and such animals increased session by session regardless of the strain The selections were made clockwise or counter-clockwise, and the direction did not change in most of the animals The rats that made such sequential selections were not considered to require a working memory for the accurate performance, and they were considered to respond sequentially intentionally Although they intended to perform such a response, the number of rats that made sequential selections decreased with SCOP injection, and the frequency of choosing the immediately adjacent arms decreased dose-dependently

Previously rats that made sequential selections were noted to resist the effect of SCOP more than the rats that did not make such sequential selection [18] However, this could not be observed in the present experiment In all strains tested, in some of the rats that made sequential selections, correct choices decreased, error choices increased and pattern of selection changed by SCOP administration And in others that made sequential selections, correct and error choices did not change but the pattern changed On the other hand, correct and error choices did not change in some of the rats that did not make sequential selections by SCOP administration However, when the rats were trained for two months with the same procedure, most rats made sequential selections for a long period and they became very resistant to SCOP as previously reported [3]

Many reports have stated that the accurate performance in this task is much impaired by the lesion of the septo-hippocampal cholinergic nervous system [16], complete aspiration of the hippocampus [7] and hippocampal injection of kinic acid [7] On the other hand, this performance has been reported to be impaired by an antero-dorsal caudate nucleus lesion [10] or the ICV injection of presynaptic cholinotoxin, AF64A [8,17]

It is well established that the cholinergic nervous systems in CNS spread mainly in three pathways in the rat from septum to cerebral cortex, hippocampus and habenula, from nucleus basalis of Meynert to frontal cortex, amygdala, and interneurons in the striatum By the IP injection of SCOP, not only the septo-hippocampal pathways, but also all these pathways, would be depressed The depressed pathways may contain the systems which mediate motivational factor or memorizing, and the performance not requiring a working memory for behaving would also be depressed

On the choice accuracy, most of the animals in all strains did not make any error choice in the first seven selections as in the final five sessions in the saline sessions, and only a few animals made error choices in the last or eighth selection However, the choice accuracy decreased especially for the

last selection in all strains dose-dependently with SCOP administration, and the number of animals that made error choices in the earlier or easier selection increased This recording measure is considered to be useful for the evaluation of detailed effects of drugs or cerebral lesions

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REFERENCES

1 Ammassari-Teule, M and A Caprioli Spatial learning and memory, maze running strategies and cholinergic mechanisms in two inbred strains of mice *Behav Brain Res* **17** 9–16, 1985
2 Bernstein, D , D S Olton, D K Ingram, S B Waller, M A Reynolds and E D London Radial maze performance in young and aged mice Neurochemical correlates *Pharmacol Biochem Behav* **22** 301–307, 1985
3 Buresova, O and J Bures Radial maze as a tool for assessing the effect of drugs on the working memory of rats *Psychopharmacology (Berlin)* **77** 268–271, 1982
4 Eckerman, D A , W A Gordon, J D Edwards, R C MacPhail and M I Gage Effect of scopolamine, pentobarbital and amphetamine on radial arm maze performance in the rat *Pharmacol Biochem Behav* **12** 595–602, 1980
5 Hiraga, Y and T Iwasaki Effects of cholinergic and monoaminergic antagonists and tranquilizers upon spatial memory in rats *Pharmacol Biochem Behav* **20** 205–207, 1984
6 Honig, W K Studies of working memory in the pigeon In *Cognitive Aspects of Animal Behavior*, edited by S H Hulse, H Fowler and W K Honig Hillsdale, NJ Lawrence Erlbaum Associates, 1978, pp 211–248
7 Jarrard, L E Selective hippocampal lesions and behavior effects of kinic acid lesions on performance of place and cue tasks *Behav Neurosci* **97** 873–889, 1983
8 Jarrard, L E , G J Kant, J L Meyerhoff and A Levy Behavioral and neurochemical effects of intraventricular AF64A administration in rats *Pharmacol Biochem Behav* **21** 273–280, 1984
9 Kuribara, H , K Ohashi and S Tadokoro Rat strain differences in the acquisition of conditioned avoidance responses and in the effects of diazepam *Jpn J Pharmacol* **26** 725, 1976
10 Masuda, Y and T Iwasaki Effects of caudate lesions on radial arm maze behavior in rats *Jpn Psychol Res* **26** 42, 1984
11 Matsumoto, A , T Kubo, S Shibanoki and K Ishihara Comparative study of rat strain difference in avoidance learning *Neurosciences (Kobe)* **12** 192–193, 1986
12 Olton, D S and R J Samuelson Remembrance of places passed spatial memory in rats *J Exp Psychol [Anim Behav]* **2** 97–116, 1976
13 Olton, D S Characteristics of spatial memory In *Cognitive Aspects of Animal Behavior* edited by S H Hulse, H Fowler and W K Honig Hillsdale NJ Lawrence Erlbaum Associates, 1978, pp 341–373
14 Olton, D S and M A Werz Hippocampal function and behavior Spatial discrimination and response inhibition *Physiol Behav* **20** 597–605, 1978
15 Stevens, R Scopolamine impairs spatial maze performance in rats *Physiol Behav* **27** 385–386, 1981
16 Walker, J A and D S Olton Spatial memory deficit following fimbria-fornix lesions Independent of time for stimulus processing *Physiol Behav* **23** 11–15, 1979
17 Walsh, T J , H A Tilson, D L DeHaven, R B Mailman, A Fisher and I Hanin AF64A a cholinergic neurotoxin, selectively depletes acetylcholine in hippocampus and cortex, and produces long-term passive avoidance and radial maze deficits in the rat *Brain Res* **321** 91–102, 1984
18 Watts, J , R Stevens and C Robinson Effects of scopolamine on radial maze performance in rats *Physiol Behav* **26** 845–851, 1981
19 Wirsching, B A , R J Beninger, K Jhamandas, R J Boegman and S R ElDefrawy Differential effects of scopolamine on working and reference memory of rats in the radial maze *Pharmacol Biochem Behav* **20** 659–662, 1984