

# A Comparison of Methylphenidate Induced Active Avoidance and Water Maze Performance Facilitation<sup>1</sup>

LOIS KINNEY<sup>2</sup> AND CHARLES V. VORHEES<sup>3</sup>

*Institute for Developmental Research, Children's Hospital Research Foundation  
Cincinnati, OH 45229*

(Received 9 December 1978)

KINNEY, L. AND C. V. VORHEES. *A comparison of methylphenidate induced active avoidance and water maze performance facilitation.* PHARMAC. BIOCHEM. BEHAV. 10(3) 437-439, 1979.—Methylphenidate was shown to facilitate both active avoidance and water maze performance compared to controls. Repetitive errors on both tasks were greater in the drug than the nondrug group and were positively correlated to water maze performance. These results fail to support the view that water maze acquisition is less influenced by performance variables than active avoidance. An unanticipated enhancement of water maze performance was also noted in the control group which had been previously tested on active avoidance compared with naive controls. Moreover, this group made fewer repetitive errors than naive controls, suggesting that previous shock exposure reduced inappropriate responses.

Methylphenidate      Active avoidance      Avoidance facilitation      Water maze      Biel maze

PSYCHOMOTOR stimulants, such as methylphenidate, have been shown to reliably facilitate performance on active avoidance tasks using shock as an aversive stimulus [8, 10, 12]. Whether such facilitation generalizes to tasks using other types of aversive stimuli has not been determined. Tasks using water escape are particularly important in this regard, not only because of the prevalence of their use, but because it has been suggested that water escape may be less subject to the influence of variables related to sex, strain and shock specific reactions [3, 6, 9, 11] that have often plagued the interpretation of active avoidance changes [1,2].

Therefore, we sought to compare the effects of a behaviorally effective dose of methylphenidate [5] to its effects on water maze acquisition. We hypothesized that methylphenidate at a dose effective in facilitating active avoidance acquisition, would not facilitate water maze acquisition. This hypothesis was based on the observation that swimming speed does not affect error rates when a treatment, such as excess vitamin A, is administered that reduces swimming speed [13].

## METHOD

### Animals

Twenty-four male rats of the Sprague-Dawley strain (Laboratory Supply, Indianapolis, Ind.) were randomly as-

signed to two experimental groups. Animals were housed individually, given ad lib food and water and tested during the light phase of the twelve hr light-dark cycle maintained in the colony.

### Apparatus

The active avoidance apparatus consisted of an aluminum chamber (20.3×21×17.8 cm) with 0.3 cm dia. grid bars spaced 1.2 cm apart that served as the floor and through which 0.75 mA of scrambled shock was delivered. The manipulandum was a 9.5 cm wide, 7.6 cm diameter wheel located at one end of the test chamber. Trials were given on a VI 45 sec schedule with a 9 sec warning stimulus of white noise which preceded shock onset. A trial was begun only after the manipulandum was not turned during a 6 sec time-out interval which preceded each trial. An avoidance occurred when a subject turned the wheel during the 9 sec warning interval.

A Biel multiple unit T-maze made of galvanized steel was used [4]. The Biel maze had a straight channel (127 cm) at the start and five T-shaped cul-de-sacs (51 cm) throughout. Water was kept at a constant depth (25.4 cm) and at a temperature of 20-22°C.

### Procedure

Rats were randomly assigned to either the methylpheni-

<sup>1</sup>Supported in part by NIH Grant HD-05221.

<sup>2</sup>Department of Psychology, University of Cincinnati, Cincinnati, OH 45221.

<sup>3</sup>Address reprint requests to Dr. Charles V. Vorhees, Division of Inborn Errors of Metabolism, Institute for Developmental Research, Children's Hospital Research Foundation, Cincinnati, OH 45229.

TABLE 1  
ACTIVE AVOIDANCE PERFORMANCE MEAN  $\pm$  SE

	Days to Criterion	Avoidances			Session Length (min)			n
		Day 1	Day 2	Day 3	Day 1	Day 2	Day 3	
Methylphenidate	1.73 $\pm$ 0.19*	13.8 $\pm$ 1.8	18.8 $\pm$ 0.4*	19.0 $\pm$ 0.4*	38.2 $\pm$ 8.5*	36.3 $\pm$ 9.5*	30.1 $\pm$ 7.8	11
Control	2.83 $\pm$ 0.32	14.2 $\pm$ 1.0	13.5 $\pm$ 0.9	16.3 $\pm$ 1.5	26.8 $\pm$ 2.8	27.9 $\pm$ 5.4	24.4 $\pm$ 3.5	12

\*Significantly different from control (see Results).

date or saline control groups. Half of each group was tested in the Biel maze first and in the active avoidance second (order 1), while the other half received the tests in the reverse order (order 2). On each day, 30 min prior to testing, drug animals were injected IP with 15 mg/kg of methylphenidate HCl (CIBA Pharmaceutical Co.) in saline (1 ml/kg). Controls received an equivalent volume of saline.

On active avoidance animals were tested for 20 trials/day until they reached a 90% avoidance criterion. Avoidances and session length were recorded. Session length was used as an index of repetitive wheel turning since session time was a function of the number of unreinforced wheel turns.

The daily training procedure on the Biel maze was as follows: On Days 1 and 2 animals were placed in one end of the 127 cm start channel with the entry to the rest of the maze blocked and timed for swimming speed to an exit ramp. Five trials/day were run, and two measures were recorded: (a) swimming time for the last two thirds of the channel, i.e., the distance best representing swimming speed and (b) total channel transit time, i.e., that which includes backtracking.

On Days 3-12 animals were placed at the start and allowed to explore the entire maze until the exit was discovered (up to a maximum of 6 min). Animals not escaping within 6 min were led to the exit by blocking inappropriate turns.

Measures recorded during Biel maze testing were (1) errors/trial, (2) time/trial, (3) error rate to criterion, i.e., the rate of decrease in errors/trial to the first errorless trial and (4) time/trial to criterion. Supplemental measures included: (5) total errors (all cul-de-sac entries), (6) T-entry errors (entries into any double cul-de-sac) and (7) repetitive errors or back-tracking, the difference between total errors and T-entry errors (essentially only a Day 1 phenomenon). If an animal took the 6 min limit to swim the maze, he was given an error score of 50.

#### Statistical Analysis

By design, methylphenidate induced avoidance facilitation was a prerequisite to the experiment, therefore, active avoidance data was analyzed using a priori *t*-tests [7]. Biel water maze data, on the other hand, where we sought to discover the effect of methylphenidate, was analyzed using treatment  $\times$  test order  $\times$  days analyses of variance. Simple two group data, such as days to criterion in avoidance, summed speed trials in the Biel maze and repetitive errors were analyzed using *t*-tests.

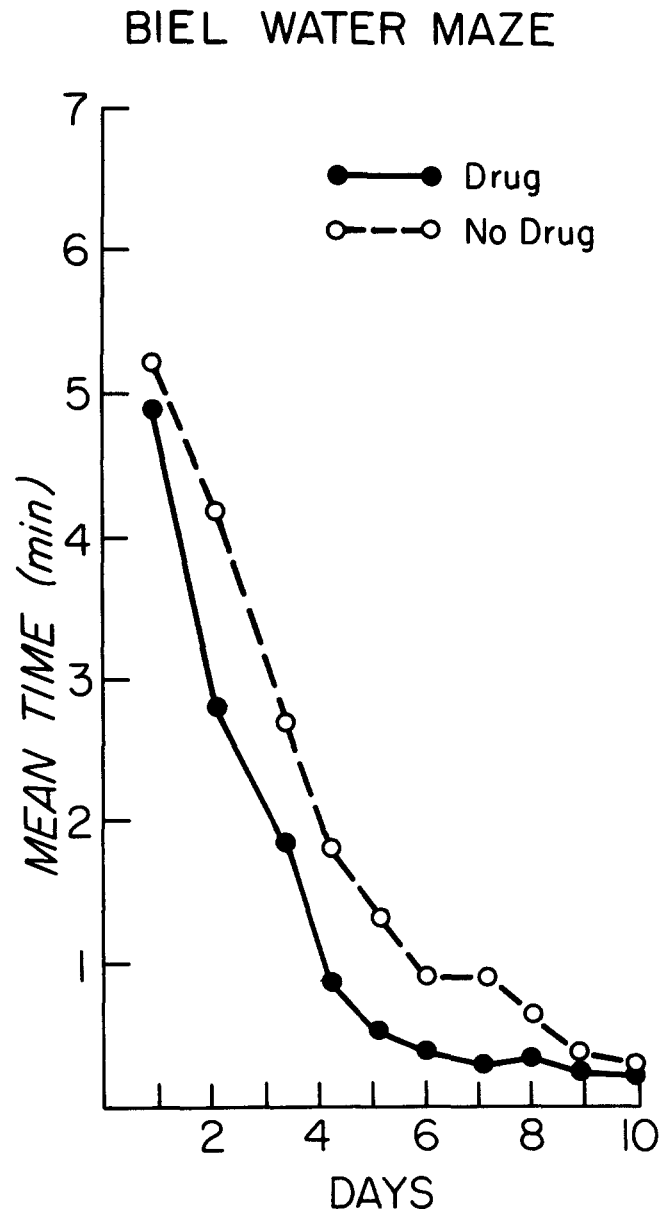


FIG. 1. Mean daily maze solution times. Overall comparison of methylphenidate (15 mg/kg/d.) compared to saline controls injected 30 min prior to a single daily maze trial.

## RESULTS AND DISCUSSION

Methylphenidate facilitated both active avoidance (Table 1) and Biel swimming maze performance (Fig. 1). On active avoidance the drug group required fewer trials to reach criterion than controls,  $t(21)=2.80$ ,  $p<0.01$ , (one methylphenidate rat died on the first day of avoidance testing and its data is excluded on this task) and made more avoidance responses on Days 2 and 3 than the nondrug group,  $t(38)=4.77$ ,  $p<0.01$ ;  $t(38)=2.43$ ,  $p<0.05$ , respectively. In the Biel maze the methylphenidate group required less time/trial,  $F(1,22)=4.39$ ,  $p<0.05$ , and made fewer errors/trial,  $F(1,22)=4.32$ ,  $p<0.05$ , than the control group (main effects). These Biel maze differences were apparently not the result of faster swimming, however, since a comparison of straight channel swim time summed across trials showed no difference in swimming speed in the final two-thirds of the alley.

The occurrence of repetitive errors (errors that did not lead to reinforcement) was greater in the drug group than in the nondrug group on both tasks. On active avoidance, the mean session length was significantly longer for the methylphenidate group compared to controls on testing day one,  $t(21)=2.95$ ,  $p<0.01$ , and two,  $t(21)=2.09$ ,  $p<0.05$ . On the Biel maze, the methylphenidate group displayed more back-tracking on straight channel trials,  $t(22)=3.40$ ,  $p<0.01$ , and committed more repetitive errors (also back-tracking) during initial maze testing than the nondrug group, errors/min:  $t(22)=1.98$ ,  $p<0.05$ . Interestingly, the correlation between back-tracking errors and learning (error rate to criterion) was significantly positive for the drug group,  $r=+0.70$ ,  $p<0.01$ , but low and negative for the nondrug group,  $r=-0.19$ , suggesting that increased activity (though not necessarily speed) contributed to the enhanced maze performance of the methylphenidate animals. This is supported by the fact that T-entry errors on the same day showed no correlation with learning rate.

Further examination of the data revealed an unexpected effect of testing order in which prior active avoidance experience facilitated performance on the swimming maze among controls. An analysis of time per trial revealed a significant drug  $\times$  test order interaction,  $F(1,20)=5.03$ ,  $p<0.05$ . This effect indicated that the control group tested in active avoidance prior to Biel maze testing performed significantly better (mean time= $1.36 \pm 0.27$ ) than controls run in the Biel maze without any prior testing (mean time= $2.14 \pm 0.29$ ). The tendency for previous shock avoidance experience to improve Biel maze performance in the nondrug group was found on all measures of Biel maze learning. Unlike facilitation due to the drug, however, facilitation due to test order appeared unrelated to an increment in the occurrence of repetitive errors, indicating that prior shock exposure affected maze performance in a different way than did methylphenidate. The control group receiving active avoidance experience first made fewer repetitive errors on the first day of learning in the Biel maze than did naive controls. In addition, the relationship between repetitive errors on Day 1 and learning (time/trial) was negative,  $r=-0.52$ , for the nondrug group, but positive for the drug group,  $r=+0.48$ . Shock exposure apparently diminished inappropriate behaviors that normally impede learning, without altering basic activity levels, whereas methylphenidate apparently altered both types of behavior. Interestingly, the beneficial carry over from one task to the other did not occur when animals were tested in the Biel maze first. This difference may be related to the species specific prepotency of swimming compared to wheel turn avoidance.

## ACKNOWLEDGEMENT

The authors would like to express their appreciation to Dr. Richard E. Butcher for his support and advice and CIBA Pharmaceuticals for their donation of Ritalin HCl.

## REFERENCES

- Barrett, R. J., N. J. Leith and O. S. Ray. Kamin effects in rats: Index of memory or shock-induced inhibition? *J. comp. physiol. Psychol.* **77**: 234-239, 1971.
- Barrett, R. J., N. J. Leith and O. S. Ray. A behavioral and pharmacological analysis of variables mediating active-avoidance behavior in rats. *J. comp. physiol. Psychol.* **82**: 489-500, 1973.
- Barrett, R. J. and O. S. Ray. Behavior in the open field, Lashley III maze, shuttle-box, and Sidman avoidance as a function of strain, sex and age. *Devl Psychol.* **3**: 73-77, 1970.
- Biel, W. C. Early age differences in the maze performance of the albino rat. *J. Genet. Psychol.* **56**: 439-453, 1940.
- Browne, R. G. and D. G. Segal. Metabolic and experimental factors in the behavioral response to repeated amphetamine. *Pharmac. Biochem. Behav.* **6**: 545-552, 1977.
- Butcher, R. E., C. V. Vorhees, C. W. Kindt, K. J. Kazmaier-Novak and H. K. Berry. Induced PKU in rats: Effects of age and melatonin treatment. *Pharmac. Biochem. Behav.* **7**: 129-133, 1977.
- Kirk, R. E. *Experimental Design: Procedures for the Behavioral Sciences*. Belmont, California: Brooks/Cole Publishing, 1968.
- Kriekhaus, E. E., N. E. Miller and P. Zimmerman. Reduction of freezing behavior and improvement of shock avoidance by d-amphetamine. *J. comp. physiol. Psychol.* **60**: 36-40, 1965.
- Polidora, V. J., R. F. Cunningham and H. A. Waisman. Phenylketonuria in rats: Reversibility of behavioral deficit. *Science* **151**: 219-221, 1966.
- Potts, W. J., D. L. Morse, B. R. Cooper and W. C. Black. The effect of magnesium pemoline, tricyanoaminopropene, and d-amphetamine on discriminated avoidance performance in rats as a function of age. *Psychon. Sci.* **20**: 141-142, 1970.
- Ray, O. S. and R. J. Barrett. Behavioral, pharmacological, and biochemical analysis of genetic differences in rats. *Behav. Biol.* **15**: 391-417, 1975.
- Rech, R. H. Amphetamine effects on poor performance of rats in a shuttle-box. *Psychopharmacologia* **9**: 110-117, 1966.
- Vorhees, C. V., R. L. Brunner and R. E. Butcher. A study of the behavioral consequences of early exposure to psychoactive drugs and animal model development. Report on contract No. 223-76-3026 to the USFDA, 1978.