Pharmacology Biochemistry & Behavior, Vol. 40, pp. 775–780. Pergamon Press plc, 1991. Printed in the U.S.A. 0091-3057/91 $3.00 + .00

Effects of Triadimefon on a Multiple Schedule of Fixed-Interval Performance: Comparison With Methylphenidate, *d*-Amphetamine and Chlorpromazine[1,2]

ANGELA R. ALLEN AND ROBERT C. MACPHAIL[3]

Department of Psychology and the Neurobiology Curriculum
University of North Carolina at Chapel Hill, Chapel Hill, NC 27514
and Neurotoxicology Division, Health Effects Research Laboratory
U.S. Environmental Protection Agency, Research Triangle Park, NC 27711

Received 20 November 1990

ALLEN, A. R. AND R. C. MACPHAIL. *Effects of triadimefon on a multiple schedule of fixed-interval performance: Comparison with methylphenidate, d-amphetamine, and chlorpromazine.* PHARMACOL BIOCHEM BEHAV **40**(4) 775–780, 1991.—Triadimefon is a fungicide that has recently been shown to increase motor activity and rates of schedule-controlled responding. These findings indicate that triadimefon resembles psychomotor stimulants and in this respect is a unique pesticide. The present experiment was designed to evaluate triadimefon's effects on performance maintained by a multiple schedule of reinforcement and to compare triadimefon to known psychomotor stimulants. Four rats were trained to perform under a mult FI 1-min FI 5-min schedule of milk reinforcement. They then received a series of dosages of triadimefon (10–170 mg/kg, IP) and of methylphenidate (1–17.3 mg/kg, IP) in a counterbalanced order. Triadimefon increased response rates in both the FI 1-min and FI 5-min components. Methylphenidate did not consistently alter response rates in either component. Temporal patterns of responding were disrupted much more in the FI 5-min component than in the FI 1-min component by both triadimefon and methylphenidate. Performances were then evaluated following a series of dosages of *d*-amphetamine (0.3–3.0 mg/kg, IP) and chlorpromazine (0.5–2.0 mg/kg, IP). Response rates were increased by *d*-amphetamine in the FI 1-min component but not in the FI 5-min component. Like triadimefon and methylphenidate, *d*-amphetamine produced a greater disruption of response patterning in FI 5-min than in FI 1-min. Only chlorpromazine decreased response rates in both components. Chlorpromazine also disrupted FI 5-min response patterning, but left FI 1-min patterning intact. Although triadimefon did not closely resemble any of the comparison drugs, it had opposite effects on response rates from chlorpromazine in both components of the schedule and resembled *d*-amphetamine in its effects on FI 1-min response rates. The rate-increasing effects frequently obtained with psychomotor stimulants were more evident for triadimefon than for either methylphenidate or *d*-amphetamine.

Triadimefon Triazole Fungicide Multiple schedule Fixed-interval *d*-Amphetamine Methylphenidate Psychomotor stimulant Chlorpromazine Rats

EVIDENCE that the triazole fungicide triadimefon may exert significant stimulant-like effects on behavior has been reported in a number of recent studies. Triadimefon has been reported to increase levels of motor activity (1, 2, 16, 19), an effect common to psychomotor stimulants such as methylphenidate and *d*-amphetamine (1,11). Large dosages of triadimefon were also recently shown to produce stereotyped behavior and alter monoamine metabolism (23) in a manner similar to that produced by *d*-amphetamine.

A characteristic stimulant-like effect on schedule-controlled behavior has also been shown to be produced by triadimefon. Stimulants frequently have effects on response rates that depend on the baseline response rates. [For an extended discussion of rate-dependency, see (12,14).] FI schedules produce a characteristic positively accelerated pattern of responses. Under an FI schedule, rate-dependency is characterized by either increased rates early in the interval, decreased rates later in the interval, or both. Moser and MacPhail (19) recently reported that tri-

[1]Portions of these data were presented at the 1987 meeting of the Southeastern Association for Behavior Analysis, and at the 1988 meeting of the Association for Behavior Analysis.

[2]The research described in this article has been reviewed by the Health Effects Research Laboratory, U.S. Environmental Protection Agency and approved for publication. Approval does not signify that the contents necessarily reflect the views and policies of the Agency nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

[3]Requests for reprints should be addressed to R. C. MacPhail, Neurotoxicology Division (MD-74B), U.S. EPA, Research Triangle Park, NC 27711.

adimefon produced rate-dependent effects on performance under a fixed-interval 3-minute (FI 3-min) schedule of reinforcement that were manifested by a disruption in the within-interval response pattern. In addition, overall rate increases were produced by triadimefon that resembled the effect of *d*-amphetamine (19).

Stimulant-like effects produced by pesticides are considered unique (2,19) since virtually all pesticides studied to date generally decrease motor activity and overall rates of schedule-controlled responding [e.g., (15)]. As a consequence, the unique effects of triadimefon described above suggested that further investigations of triadimefon's behavioral effects were warranted. The present study was designed with several aims. First, it was designed to extend the effects reported by Moser and MacPhail (19) to testing conducted with a multiple schedule. It was also designed in order to systematically compare triadimefon's effects on response rate and patterns in the two intervals, and to examine effects of triadimefon on response patterns in some detail. Finally, this study was designed to compare triadimefon's effects to the effects of the psychomotor stimulants methylphenidate and *d*-amphetamine.

A multiple fixed-interval one-minute fixed-interval five-minute (mult FI 1-min FI 5-min) schedule was used for this study. This schedule permits study of the effects of triadimefon and comparison drugs on overall response rates, as well as within-interval (local) response rates which reflect the pattern of responding within each interval. Interval lengths were chosen so as to be both shorter (FI 1-min) and longer (FI 5-min) than the FI 3-min schedule used by Moser and MacPhail (19). A mult FI 1-min FI 5-min schedule has been used previously to study the behavioral effects of several formamidine pesticides (18) and thus use of this schedule afforded the opportunity to compare triadimefon to a different class of pesticides. Methylphenidate was chosen as a comparison drug because it has been reported to increase motor activity (1, 5, 7) and to produce rate-dependent effects on schedule-controlled behavior (3, 4, 10, 21). *d*-Amphetamine was also included as another psychomotor stimulant which has effects similar to methylphenidate. Finally, rats were tested with chlorpromazine so that the effects of triadimefon, methylphenidate, and *d*-amphetamine could be compared to those of a nonstimulant psychoactive drug.

METHOD

Subjects

Four experimentally naive male Long-Evans hooded rats (Charles River, Portage, MI), 75 days old at the onset of training, served as subjects. Rats were individually housed in suspended Plexiglas cages with direct bedding. A 12-hour daily light cycle (6:00 a.m. to 6:00 p.m.) was in effect in the animal colony room. Food (Purina Rat Chow) availability was limited to maintain body weights at approximately 350 grams. Water was available ad lib in the home cage.

Apparatus

Four operant chambers (Coulbourn Instruments Model E10-10) equipped with a mechanism for milk presentation were used. Illumination of either three multicolored cue lights mounted above the lever (FI 1-min) or a houselight mounted near the top middle of the front panel (FI 5-min) served as discriminative stimuli. Reinforcement consisted of 4-s access to approximately 0.05 ml of milk (one part Eagle Brand sweetened condensed milk to two parts water). The experimental procedures and data collection were programmed using a SKED-11 software system (State Systems Inc.).

Procedure

Training. The rats were given ad lib food until their individual body weights reached 350 grams. Food was then restricted to maintain them at that body weight. Training sessions began 3–4 days later. All training and subsequent sessions were carried out five days a week, Monday through Friday. During dipper training, rats were given random one-minute access periods to a dipper containing milk. Lever presses also produced milk. The duration of dipper presentations was gradually reduced to four seconds. The rats were then exposed to a modified autoshaping procedure in which the cue lights above the lever were illuminated for eight seconds prior to milk presentation. Lever presses also produced milk. All rats were consistently pressing the lever after about three days on this procedure.

Baseline. A multiple FI 1-min FI 5-min schedule with a limited hold of 60-s in each component was then initiated. These sessions lasted approximately 70 minutes. Each component was presented ten times, beginning with FI 1-min, and was separated from the next component by 15-s timeout periods. Reinforcement occurred following the first response after the interval elapsed. If no response occurred within 60 s of reinforcement availability, the component ended automatically (limited hold 60 s). A total of twenty reinforcers per session was therefore available. Responding during timeout had no scheduled consequences except during the last three seconds when a response prolonged the timeout by one second. Dosing was initiated upon stabilization of performance (86 training sessions).

Drug preparation and administration. Triadimefon (Chem Service, Inc., Westchester, PA) was finely ground and suspended in a 5% ethanol, 5% Emulphor, 90% saline vehicle. Methylphenidate hydrochloride, *d*-amphetamine sulfate and chlorpromazine hydrochloride (all from Sigma Chemical Co., St. Louis, MO) were dissolved in physiological saline. Dosages of triadimefon (10, 30, 56, 100 and 170 mg/kg) or vehicle were administered IP 60 minutes prior to the session. Dosages of saline, methylphenidate (1.0, 3.0, 10.0 and 17.3 mg/kg), *d*-amphetamine (0.3, 1.0, 1.7 and 3.0 mg/kg), and chlorpromazine (0.5, 1.0 and 2.0 mg/kg) were administered IP 20 minutes prior to the session. Dosages of these latter three were based on the salt weight of the compounds. Concentrations were adjusted so that all injections were given in a volume of 1 ml/kg. An exception was the 170 mg/kg dosage of triadimefon, which was given in 2 ml/kg because of solubility problems. Dosing usually took place on Tuesdays and Fridays. Thursdays served as noninjected control sessions. When rates or patterns of responding were noticeably disrupted on sessions following dosage days, dosing was suspended until baseline performances were recovered. All dosages of one compound were administered before dosing with another compound was initiated.

Dosages of triadimefon and methylphenidate preceded *d*-amphetamine and chlorpromazine. Dosing was counterbalanced such that rats 9 and 10 received methylphenidate before triadimefon, while the reverse order was used for rats 11 and 12. Each dosage of triadimefon and methylphenidate was administered two or three times, except 170 mg/kg of triadimefon (see below). Each of the vehicles was also administered three to four times during these dosage-response determinations. Several weeks of drug-free testing took place between the triadimefon and methylphenidate regimens. About one week following completion of these dosage-response determinations the effects of *d*-amphetamine and then chlorpromazine were determined in each rat.

Dosing procedures were identical to those for triadimefon and methylphenidate except each dosage was given only once. Three saline-injection sessions provided vehicle-control data for evaluating the effects of both *d*-amphetamine and chlorpromazine. At the end of the *d*-amphetamine and chlorpromazine determinations, 170 mg/kg of triadimefon was administered to each rat.

Data Analysis

Overall response rates were calculated as the number of responses for each rat in each component divided by the time spent in that component. Data were then converted to percent-of-vehicle by dividing the mean response rate for each component at each dosage by the mean vehicle control response rate for that component. Data were then averaged across rats.

Within-interval response patterning was expressed by the index-of-curvature (IOC) statistic of Fry et al. (8). Positive IOC values reflect positively accelerated responding within the fixed interval. An IOC value of zero reflects constant responding throughout the interval, and negative IOC values reflect negatively accelerated responding within the interval. Responses were totaled in tenths of each interval, and therefore the range of attainable IOC values was from -0.9 to 0.9 (8). Mean IOC values were obtained by calculating the mean IOC for each dosage for each rat and then averaging across rats. IOC values for a component were not calculated for sessions when response rates for that component were less than 1/min, as IOC becomes an inaccurate measure of patterning when only a few responses are emitted.

Means and standard errors of the mean (SEM) were calculated for each dosage. Treatment data were considered significant if one SEM of the treatment data did not overlap one SEM of the vehicle-injected control sessions (response rate data) or one SEM of both the noninjected and vehicle-injected control sessions (IOC data).

RESULTS

Baseline Performance

Baseline (vehicle-control) rates of overall responding in FI 1-min exceeded FI 5-min rates, but IOC values were virtually the same for both components (see Table 1 for individual rats' data and group averages). These vehicle-control values were similar to noninjected control data, and were used to evaluate the effects of the various chemicals on performance. Some shifts in vehicle-control values were evident between the triadimefon/methylphenidate determinations and the *d*-amphetamine/chlorpromazine determinations. These values are therefore reported separately in Table 1.

Effects on Overall Response Rates

Triadimefon increased overall rates of responding except at the 170 mg/kg dosage, which decreased rates to near zero (see Fig. 1). Dosage-response functions were remarkably similar for the two schedule components. Methylphenidate produced no significant changes in response rate in either component. *d*-Amphetamine increased then decreased response rates in the FI 1-min component, but left response rates in the FI 5-min component unaffected or decreased. Chlorpromazine only decreased response rates in both components. In summary, rate increases were only produced by triadimefon in both components and by *d*-amphetamine in the FI 1-min component. Chlorpromazine produced effects opposite those of triadimefon.

Effects on Response Patterns

Response patterning was unaffected by triadimefon in the FI 1-min component (see Fig. 2). In contrast, triadimefon severely disrupted FI 5-min response patterning. No IOC values could be calculated for 170 mg/kg triadimefon. Details of triadimefon's

TABLE 1

VEHICLE CONTROL DETERMINATIONS

	Triadimefon/Methylphenidate		*d*-Amphetamine/Chlorpromazine	
	Rate	IOC	Rate	IOC
S9:				
FI 1-min	35.1 ± 2.7*	0.64 ± 0.01	14.5 ± 3.3	0.76 ± 0.02
FI 5-min	14.3 ± 1.4	0.63 ± 0.03	20.9 ± 2.7	0.67 ± 0.01
S10:				
FI 1-min	11.2 ± 0.9	0.69 ± 0.02	12.9 ± 0.5	0.73 ± 0.01
FI 5-min	2.9 ± 0.3	0.54 ± 0.03	4.3 ± 0.3	0.66 ± 0.02
S11:				
FI 1-min	16.5 ± 1.7	0.45 ± 0.03	15.3 ± 1.9	0.64 ± 0.03
FI 5-min	4.8 ± 0.8	0.46 ± 0.05	3.3 ± 0.7	0.50 ± 0.04
S12:				
FI 1-min	11.7 ± 1.9	0.31 ± 0.06	17.1 ± 1.5	0.48 ± 0.01
FI 5-min	3.8 ± 0.6	0.47 ± 0.06	5.7 ± 0.6	0.66 ± 0.03
Group Mean:				
FI 1-min	18.6 ± 5.6	0.52 ± 0.09	15.0 ± 0.9	0.65 ± 0.06
FI 5-min	6.5 ± 2.6	0.53 ± 0.04	8.6 ± 4.1	0.63 ± 0.04

*Values for individual subjects are means plus or minus one standard error of the mean based on averages of vehicle and saline (triadimefon/methylphenidate) values or averages of saline (*d*-amphetamine/chlorpromazine) values.

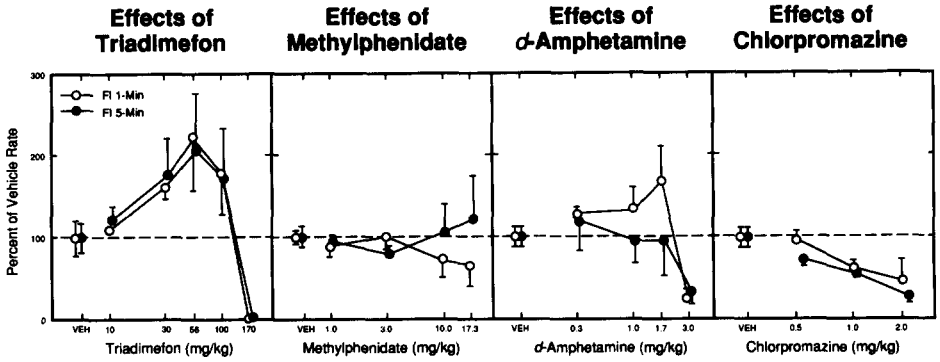

FIG. 1. Effects of triadimefon (first panel), methylphenidate (second panel), *d*-amphetamine (third panel), and chlorpromazine (fourth panel) on overall FI 1-min (open symbols) and FI 5-min (closed symbols) response rates. Data are expressed as the percent of vehicle (VEH) control rates, averaged across rats (N = 4). Vertical bars represent one standard error of the mean. Dashed line represents 100% of vehicle control rates.

effects on response patterning are presented in Fig. 3 for individual rats. A dosage of 100 mg/kg triadimefon produced proportionately greater increases in the local rates that occurred early in the interval than in the higher rates that occurred later in the interval. The greater increases in local rates in FI 5-min than in FI 1-min were responsible for the decrease in FI 5-min IOC.

Methylphenidate only disrupted response patterning in the FI 1-min component at the two highest dosages. Greater disruption at the three highest dosages occurred in the FI 5-min component. *d*-Amphetamine also disrupted response patterning in the FI 1-min component at the two highest dosages and in the FI 5-min component at all dosages. Chlorpromazine did not affect response patterning in the FI 1-min component but disrupted response patterning in the FI 5-min component. In summary, all compounds substantially disrupted FI 5-min patterning in a dosage-dependent manner but had either little or no effect on FI 1-min patterning.

DISCUSSION

The present experiment revealed reliable effects of triadimefon on the overall response rates and the pattern of responses maintained by two different fixed-interval schedules of reinforcement. After triadimefon, response rates were increased to an equal degree in both components, but disruption of response patterning occurred only in the FI 5-min component. This disruption is consistent with a rate-dependent account of triadimefon's effects, since within-interval response rate data revealed an orderly relationship between local rates of responding under control conditions and the corresponding local rates after 100 mg/kg triadimefon, especially in the FI 5-min component. Triadimefon-induced changes in response patterning were not related to baseline patterning, as baseline IOC values were virtually equal in both components. The alterations in response patterning occurred regardless of the effect of triadimefon on overall response rates.

The effects of the comparison stimulants, methylphenidate and *d*-amphetamine on response rates were dissimilar to each other and except for effects of *d*-amphetamine on FI 1-min responding, dissimilar to triadimefon. FI response rate increases have been previously reported for *d*-amphetamine (19,22) in rats although exceptions exist [i.e., (10)]. Methylphenidate did not increase response rates, but other studies have reported no FI response rate increases caused by methylphenidate (10, 21, 24). Chlorpromazine, unlike the other three compounds, only decreased response rates in both components.

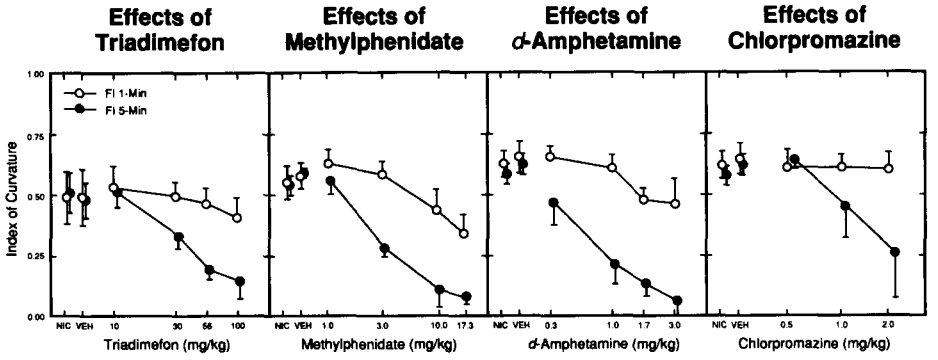

FIG. 2. Effects of triadimefon (first panel), methylphenidate (second panel), *d*-amphetamine (third panel), and chlorpromazine (fourth panel) on overall FI 1-min (open symbols) and FI 5-min (closed symbols) index of curvature values. Data are expressed as group averages (N = 4). Vertical bars represent one standard error of the mean.

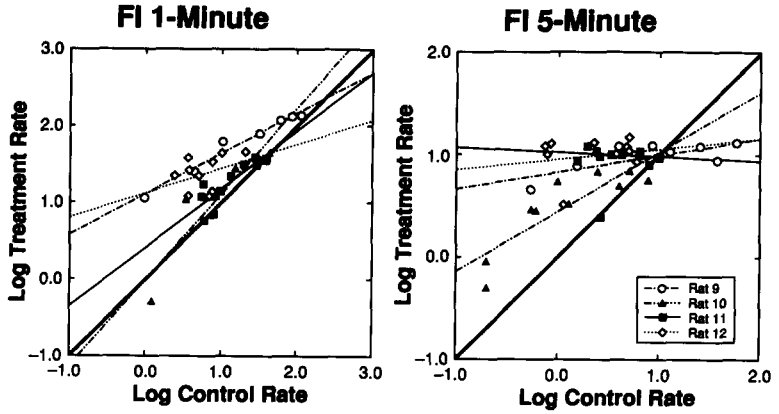

FIG. 3. Effects of 100 mg/kg triadimefon on local rates of responding in FI 1-min (left panel) and FI 5-min (right panel). The logarithm of rates in successive tenths of the interval after 100 mg/kg triadimefon is plotted as a function of corresponding logarithm of local rates after vehicle. Scale differences in the axes of the two panels should be noted. The diagonal line represents no change from vehicle. Each symbol and line represents data from a single rat, and are based on the mean of all administrations for each rat of 100 mg/kg triadimefon and vehicle.

The effects of triadimefon on overall response rates are different from those of most pesticides that have been studied. Pesticides typically have been found to decrease overall rates of schedule-controlled responding under a variety of conditions [e.g., (9, 13, 15, 17, 18)]. For instance, Moser and MacPhail (18) examined the effects of formamidine pesticides (chlordimeform, amitraz and formetanate) on the responding of rats under a mult FI 1-min FI 5-min schedule. All three formamidines generally decreased overall response rates in a dosage-related manner. Pattern disruptions were produced by two of the pesticides, but these occurred only at the highest dosages. This profile of effects is quite distinct from that produced in the present experiment by triadimefon.

The present study found effects of triadimefon similar to those reported previously (19). That study utilized a single FI schedule and reported response rate increases and pattern disruption as a result of triadimefon, and response rate increases as a result of *d*-amphetamine. The present study utilized a multiple schedule and found that similarities between triadimefon and *d*-amphetamine were evident in the FI 1-min component of the schedule. However, triadimefon also increased response rates in the FI 5-min component, whereas *d*-amphetamine did not. Therefore, in this experiment triadimefon's rate-increasing effects on FI performance were more consistent that those of *d*-amphetamine.

There are implications for stimulant properties of triadimefon. Triadimefon was more effective in increasing overall rates of responding than either of the stimulants used in this experiment. This behavioral action raises the possibility that triadimefon may have risk factors characteristic of other rate-increasing compounds, such as cardiovascular and cognitive effects (6,25). The unusual behavioral properties of triadimefon may also extend to other triazole fungicides. At least one other triazole fungicide, triadimenol, has been found to increase motor activity (16). Further work is needed to characterize the effects of triazole fungicides on schedule-controlled performance.

ACKNOWLEDGEMENTS

The authors thank Drs. William Boyes, Linda Dykstra and David Eckerman for critically reviewing this manuscript. Special thanks are due to the late Dr. David B. Peele for his invaluable help with contingency and data-analysis programming, and review of this manuscript.

REFERENCES

1. Crofton, K. M.; Boncek, V. M.; MacPhail, R. C. Evidence for aminergic involvement in triadimefon-induced hyperactivity. Psychopharmacology (Berlin) 97:326–330; 1989.
2. Crofton, K. M.; Boncek, V. M.; Reiter, L. W. Hyperactivity induced by triadimefon, a triazole fungicide. Fundam. Appl. Toxicol. 10:459–465; 1988.
3. Eckerman, D. A.; Segbefia, D.; Manning, S.; Breese, G. S. Effects of methylphenidate and *d*-amphetamine on timing in the rat. Pharmacol. Biochem. Behav. 27:513–515; 1987.
4. Emmett-Oglesby, M. W.; Taylor, K. E.; Dafter, R. E. Differential effects of methylphenidate on signalled and nonsignalled reinforcement. Pharmacol. Biochem. Behav. 13:467–470; 1980.
5. Fessler, R. G.; Sturgeon, R. D.; Meltzer, H. Y. Effects of phencyclidine and methylphenidate on *d*-amphetamine-induced behaviors in reserpine-pretreated rats. Pharmacol. Biochem. Behav. 13:835–842; 1979.
6. Franz, D. N. Central nervous system stimulants. In: Gilman, A. G.; Goodman, L. S.; Rall, T. W.; Murad, F., eds. Goodman and Gilman's The pharmacological basis of therapeutics. New York: Macmillan Publishing Co.; 1985:582–588.
7. Freeman, G. B.; Wallace, R. B.; Werboff, J.; Root, R. B.; Smith, P.; Warner, N. W. Activity analysis of operant behavior following methylphenidate administration. Percept. Mot. Skills 47:163–167; 1978.
8. Fry, W.; Kelleher, R. T.; Cook, L. A mathematical index of performance on fixed-interval schedules of reinforcement. J. Exp. Anal. Behav. 3:193–199; 1960.
9. Glowa, J. R. Acute and subacute effects of deltamethrin and chlordimeform on schedule-controlled responding in the mouse. Neurobehav. Toxicol. Teratol. 8:97–102; 1986.
10. Harris, R. A.; Snell, D.; Loh, H. H. Effects of stimulants, anorectics, and related drugs on schedule-controlled behavior. Psychopharmacology (Berlin) 56:49–55; 1978.
11. Kelleher, R. T. Psychomotor stimulants. In: Pradhan, S. N.; Dutton, S. N., eds. Drug abuse: The clinical and basic aspects. St. Louis: C. V. Mosley Co.; 1977:116–147.

12. Kelleher, R. T.; Morse, W. H. Determinants of the specificity of behavioral effects of drugs. Ergeb. Physiol. Biol. Chem. Exp. Pharmacol. 60:1–56; 1968.
13. Leander, J. D.; MacPhail, R. C. Effect of chlordimeform (a formamidine pesticide) on schedule-controlled responding of pigeons. Neurobehav. Toxicol. 2:315–321; 1980.
14. McKearney, J. W. Rate dependency: Scope and limitations in the explanation and analysis of the behavioral effects of drugs. Adv. Behav. Pharmacol. 3:91–109; 1981.
15. MacPhail, R. C. Effects of pesticides on schedule-controlled behavior: In: Seiden, L. S.; Balster, R. L., eds. Behavioral pharmacology: The current status. New York: Alan R. Liss, Inc.; 1985: 519–535.
16. MacPhail, R. C. Unexpected psychomotor stimulant-like effects of triadimefon and triadimenol in mice. Paper presented at the 1986 annual meeting of the Behavioral Toxicology Society.
17. MacPhail, R. C.; Leander, J. D. Chlordimeform effects on schedule-controlled behavior in rats. Neurobehav. Toxicol. Teratol. 3:19–26; 1981.
18. Moser, V. C.; MacPhail, R. C. Differential effects of formamidine pesticides on fixed-interval behavior in rats. Toxicol. Appl. Pharmacol. 84:315–324; 1986.
19. Moser, V. C.; MacPhail, R. C. Neurobehavioral effects of triadimefon, a triazole fungicide, in male and female rats. Neurotoxicol. Teratol. 11:285–293; 1989.
20. Randrup, A.; Munkvad, I. Biochemical, anatomical and psychological investigations of stereotyped behavior induced by amphetamines. In: Costa, E.; Garattini, S., eds. Amphetamines and related compounds: Proceedings of the Mario Negri Institute for Pharmacological Research, Milan, Italy. New York: Raven Press; 1970:695–713.
21. Sagvolden, T.; Jenssen, J. R.; Brorson, I. W. Rate-dependent effects of methylphenidate (Ritalin) on fixed-interval behavior in rats. Scand. J. Psychol. 24:231–236; 1983.
22. Segal, S. A.; Moerschbaecher, J. M.; Thompson, D. M. Effects of phencyclidine, *d*-amphetamine and pentobarbital on schedule-controlled behavior in rats. Pharmacol. Biochem. Behav. 15:807–812; 1981.
23. Walker, Q. D.; Lewis, M. H.; Crofton, K. M.; Mailman, R. B. Triadimefon, a triazole fungicide, induces stereotyped behavior and alters monoamine metabolism in rats. Toxicol. Appl. Pharmacol. 102:474–485; 1990.
24. Wayner, M. J.; Mintz, R. B.; Jolicoeur, F. B.; Rondeau, D. B. Effects of methylphenidate on schedule-dependent and schedule-induced behavior. Pharmacol. Biochem. Behav. 10:299–302; 1979.
25. Weiner, N. Norepinephrine, epinephrine, and the sympathomimetic amines. In: Gilman, A. G.; Goodman, L. S.; Rall, T. W.; Murad, F., eds. Goodman and Gilman's The pharmacological basis of therapeutics. New York: Macmillan Publishing Co.; 1985:145–180.