The effects of illumination, d-amphetamine, and methylphenidate upon vigilance performance of squirrel monkeys

EUGENE R. DELAY
Regis College, Denver, Colorado 80221

and

WALTER ISAAC
University of Georgia, Athens, Georgia 30602

The effects of illumination, d-amphetamine, and methylphenidate on vigilance behavior were studied with four squirrel monkeys. Detection rates of an auditory signal were higher in the light than in the dark. Although methylphenidate did not alter performance, d-amphetamine lowered detection rates more in the light than in the dark, particularly in male squirrel monkeys. Results were interpreted in terms of altered arousal levels.

Vigilance has been defined as "a state of readiness to detect and respond to certain specified small changes occurring at random time intervals in the environment" (N. H. Mackworth, 1957, p. 389). The importance of arousal, one of the many variables thought to effect such behavior, has been recognized in several theoretical papers (Frankmann & Adams, 1962; Hebb, 1955; Lindsley, 1960; Scott, 1966; Stroh, 1971). It has been demonstrated that cortical arousal can be altered with sensory stimulation via the reticular formation (Starzl, Taylor, & Magoun, 1951), and it was this functional aspect of sensory input that Hebb (1955) felt was necessary for an organism to maintain an alert, vigilant state. Isaac and Devito (1958) have suggested that behavioral manifestations of arousal could be influenced by varying the intensity of ambient sensory conditions in the environment.

Numerous studies have since reported that vigilance behavior in humans is sensitive to the effects of noise, and, generally, investigators have found that increasing either the intensity or the variability of auditory stimulation has enhanced performance (Davenport, 1972; Davies & Hockey, 1966; Kirk & Hecht, 1963; McGrath, 1963; Watkins & Feehrer, 1965). Thus far, however, no one has investigated what effect ambient illumination may have upon vigilance behavior. Previous studies with diurnal animals have shown that ambient illumination increases locomotor activity (Alexander & Isaac, 1965;

Isaac & Troelstrup, 1969) and fixed-interval responding (Isaac, 1969; Stinnette & Isaac, 1975), suggesting that light has an excitatory effect upon behavior in diurnal animals. Therefore, it would seem likely that ambient illumination may influence vigilance behavior as well.

Another means of altering arousal is through the use of pharmacological agents such as dextroamphetamine, or Dexedrine (Bradley & Key, 1958), a drug that has been classified as a CNS stimulant (Goodman & Gilman, 1975). However, the behavioral effects of d-amphetamine do not appear to be simple. For example, Isaac and Troelstrup (1969) found that while d-amphetamine increased locomotor activity in nocturnal owl monkeys, the drug decreased activity in diurnal squirrel monkeys. Furthermore, these investigators reported that the drug altered the activity of both species only when ambient illumination was present in the environment. Alexander and Isaac (1965) have suggested that d-amphetamine produces a depressant effect on the behavior of diurnal animals by reducing the effects of ambient illumination.

Previous studies have suggested that d-amphetamine and another drug classified as a CNS stimulant (Goodman & Gilman, 1975), methylphenidate hydrochloride (Ritalin), may have similar effects on behavior. In a study comparing the effects of these drugs on activity of albino rats, Kallman and Isaac (1975) found that the level of ambient illumination also influenced the potency of methylphenidate. Both drugs elevated activity more in the light than in the dark, although methylphenidate required nearly twice the dosage (milligrams per kilogram of body weight) to produce behavioral changes equivalent to those seen with d-amphetamine. Further, Davis (1957) administered racemic amphetamine and methylphenidate subcutaneously and found that these two drugs reduced pacing behavior in rhesus monkeys in a similar fashion.

0090-5054/80/040203-04$00.65/0

Methylphenidate and d-amphetamine have also been reported to alter responding on tasks requiring prolonged attention, or vigilance. Reviews by Barkley (1977) and Whalen and Henker (1976) indicated that methylphenidate and d-amphetamine appeared to improve the performance of hyperkinetic children on attentional tasks. However, studies examining the effects of these drugs in adult humans either have not been able to find an effect on vigilance behavior (Hink, Fenton, Tinklenberg, & Kopell, 1978) or have used only a single, low dose (Loeb, Hawkes, Evans, & Alluisi, 1965; J. F. Mackworth, 1965), making it difficult to interpret what effects these drugs may have on vigilance behavior

The present study attempted to systematically investigate the effects that illumination, d-amphetamine, and methylphenidate may have on vigilance performance of diurnal squirrel monkeys. If increasing the intensity of ambient illumination enhances behavior in diurnal animals, as suggested by previous studies, it would be predicted that vigilance performance should be better in the light than in the dark. If, on the other hand, d-amphetamine reduces the effect of illumination on behavior, then the drug should produce its greatest effect when the animals are tested in the light and should produce dose-related decrements in vigilance performance of diurnal animals. Similar predictions would be made for methylphenidate if it affects behavior in a manner similar to d-amphetamine.

METHOD

Subjects

The subjects were four squirrel monkeys (*Saimiri sciureus*), two males and two females, which were 2.5 years old at the beginning of the experiment. All animals had previous experience with d-amphetamine and methylphenidate as part of an experiment measuring the effects of these drugs on auditory thresholds (Delay, Steiner, & Isaac, 1979). The animals were housed in heterosexual pairs in the colony and maintained on a 12-h light, 12-h dark cycle with the lights turned on at 5:00 a.m. All animals were tested at the same time each day between 9:00 a.m. and 12:00 noon. All animals were maintained at normal body weight throughout the experiment, with food and water available ad lib in the home cage. The animals were weighed at the beginning of each replication and at the end of the study.

Apparatus

The animals were transported to the experimental apparatus and tested in an expanded metal transport cage 24.4 cm high, 24.4 cm wide, and 38.5 cm long. The doors at both ends of the transport cage were made of Plexiglas, painted black. An operant lever, which served both as a response manipulandum and as the reinforcement site, was inserted into a small opening in one of the doors. The lever was illuminated internally with a dim light throughout all test sessions (Davis Scientific Instruments, BD-2). The transport cage was placed inside a sound-attenuated wooden chamber. The chamber measured 53 cm high, 55 cm wide, and 71 cm deep inside and was painted flat white. A fluorescent light was recessed in the chamber ceiling directly over the center of the transport cage and was covered with frosted glass. The door of the chamber had a 28 x 43 cm Thermopane observation window covered with cheese cloth on the outside. A ventilation fan provided 68-dB ambient noise (A scale, re: 20 μN/M^2). The auditory stimulus was a 4-kHz tone, 500 msec in duration and approximately 8-10 dB above

each animal's threshold in the light. The tone was generated by solid state circuitry (Delay, Golden, & Steiner, 1978) and was delivered through an 8-ohm speaker to the inside of the chamber 45 cm from the center of the transport cage. All programming and recording equipment was located in a separate room.

Procedure

Light (376.74 lx) and dark (less than 10.76 lx) ambient sensory conditions were alternated daily. The animals spent the first 10 min of the 70-min vigilance session adapting to the illumination level. Four warm-up trials were presented during the last 5 min of the adaptation period, but they were not included in the analysis. The remaining 60 min were divided into four 15-min intervals. Six stimuli were randomly presented in each interval, with a mean of 2.5 min between stimulus presentations. The total number of correct responses for each interval was recorded to evaluate the effects of elapsed time on performance.

A trial was 3 sec in duration, with the stimulus present during the first .5 sec. A correct response, or detection, was a leverpress emitted at any point during the trial. This response terminated the trial and delivered 1/8 cc of the reinforcer (sweetened Hawaiian Punch). Incorrect responses, or false alarms, were recorded cumulatively for a complete experimental session, with the exception of responses made during a 10-sec period following the delivery of the reinforcer. This prevented recording leverpresses resulting from the animal's obtaining the reinforcer. In addition, false alarms emitted during the 10 sec prior to the stimulus onset resulted in delaying the onset of the stimulus for 10 sec ensuring stimulus control and a low false alarm rate.

The animals were trained on the task until they were able to detect 80% of the stimulus presentations during the first interval in the light. When the animals met this criterion on 5 consecutive days in the light, drug administration was begun. One male and one female began the experiment with d-amphetamine; the other two animals started with methylphenidate. Each of four doses of d-amphetamine (.0, .1, .2, and .4 mg/kg) and four doses of methylphenidate (.0, .4, .8, and 1.6 mg/kg) were prepared in constant-volume solutions. Bacteriostatic water was used as the placebo solution and was the vehicle for all drug doses. A single dose was administered orally in 10 cc of sweetened Hawaiian Punch 5 min prior to placing the animals in the apparatus. The sequence of doses for each drug was determined for each animal by using a Latin square. A different sequence was used for each illumination condition and for each replication. Therefore, a replication consisted of 1 day for each drug level under each illumination condition, for a total of 8 days per replication. The animals were adapted to the taste of each drug as well as the peripheral effects of the drug during the first two replications with the drug. Data from three subsequent replications were evaluated by analysis of variance. At the end of the last replication with the first drug, the animals had a 5-day period during which the experimental procedures were continued but no drug was given. At the end of this period the animals began a new series of replications with the second drug. Again, the first two replications were for adaptation, and the next three were used for analysis. Thus, each animal had five replications with the second drug. In this fashion all animals were tested under both drug conditions.

RESULTS

Data from each drug condition were analyzed using a five-factor analysis of variance, with sex as an independent factor and repeated measures on illumination, dose, intervals, and replications (see Figure 1). The analysis of the d-amphetamine data indicated that the drug produced a significant dose-related decrease in
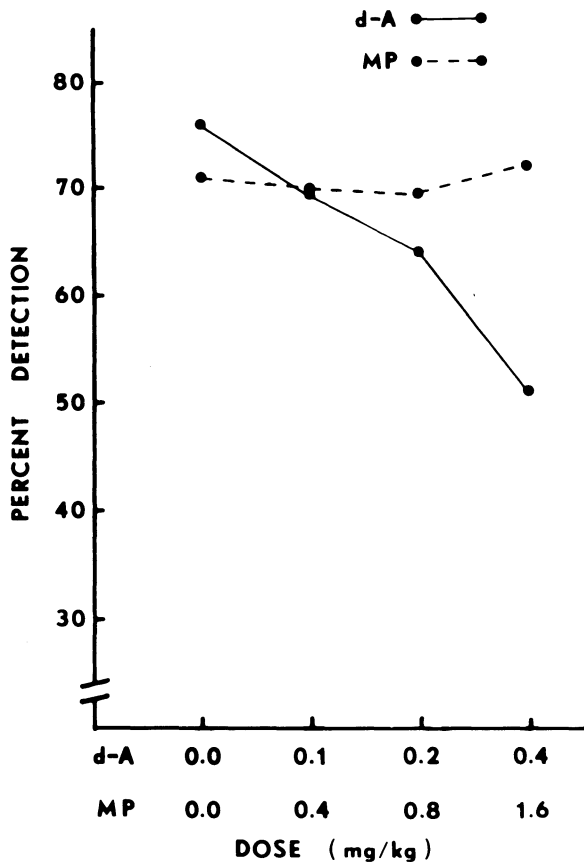
Figure 1. The effects of increasing doses of d-amphetamine (d-A) and methylphenidate (MP) on detection.

DISCUSSION

Hebb (1955) has suggested that it is the arousal aspect of sensory stimulation that is essential for the maintenance of a vigilance state. The intensity of sensory stimulation has been hypothesized as a major stimulus characteristic affecting the arousal level of an organism (Isaac & Devito, 1958). Studies have generally shown that human subjects are more proficient on a variety of visual vigilance tasks when the intensity of ambient noise is increased or made variable (Davenport, 1972; Davies & Hockey, 1966; Kirk & Hecht, 1963; McGrath, 1963; Watkins & Feehrer, 1965). In this study, detection rates of an auditory stimulus were higher in the light than in the dark, indicating that the intensity of ambient light can influence performance on attentional tasks. Previously reported data on locomotor activity (Alexander & Isaac, 1965; Isaac & Troelstrup, 1969), fixed-interval responding (Isaac, 1969; Stinnette & Isaac, 1975), sensory thresholds (Delay, Smith, & Isaac, 1978), and reaction times (Hornbuckle, 1972; Kallman & Isaac, 1977) have suggested that diurnal animals are more aroused in the light than in the dark. It would appear from this study that the presence of ambient illumination and consequent increased arousal level can facilitate performance of diurnal animals on a vigilance task as well.

A performance decrement over time has generally been reported in vigilance studies, particularly if the ambient sensory conditions are uniform throughout the session (Stroh, 1971). Scott (1966) has suggested that this decrement is due to sensory habituation, resulting in a decrease in arousal level. The decrements in detection rates across intervals in the present study are in agreement with this notion.

Although d-amphetamine appears to have a stimulant effect on behavior in nocturnal animals (Isaac & Troelstrup, 1969; Kallman & Isaac, 1975; Seegal & Isaac, 1971), the drug has been found to decrease locomotor activity (Alexander & Isaac, 1965; Davis, 1957; Isaac & Troelstrup, 1969; Lowther & Isaac, 1976) and to reduce fixed-interval responding (Goethe & Isaac, 1977; Stinnette & Isaac, 1975) in diurnal animals. In the presence of light, d-amphetamine has also consistently been shown to have its greatest effect on behavior (Isaac & Troelstrup, 1969; Lowther & Isaac, 1976; Stinnette & Isaac, 1975). Alexander and Isaac (1965) posited that d-amphetamine may have the same effect on arousal as reducing ambient visual input and, therefore, would appear to act as a depressant on behavior in diurnal animals. The dose-related decrement in detection rate seen primarily in the light in this study is consistent with this notion. This decrement was greater for the males than for the females, which is consistent with previous findings (Stinnette & Isaac, 1975) that males appear to be more responsive to the drug than females.

Although false alarms also showed a dose-related reduction, it would seem unlikely that a lower response rate could account for all of the changes in detection rate. First, a 10-sec delay in the trial onset was imposed if a response was emitted within 10 sec preceding the stimulus presentation, ensuring stimulus control of the leverpress response. The false alarm rate was less than 2/min even under the placebo condition, a rate unlikely to influence the detection rate by producing a response during a trial lasting only 3 sec and occurring on the average of once every 2.5 min. Second, detection rate was altered by d-amphetamine as a result of the drug's interacting with the level of illumination and the sex of the animal, whereas only d-amphetamine altered false alarm responding. This suggests that d-amphetamine reduced detection rate independently of any changes in false alarm responding.

Methylphenidate did not have an effect on vigilance performance in the present study. This was surprising, since all the doses used in this study have been shown to produce behavioral effects in other organisms. Werry (1976) reported that most children are responsive to methylphenidate at doses as low as .3 mg/kg. Changes in locomotor activity have also been observed

detection rate $[F(3,190) = 16.45, p < .005]$. The analysis also revealed significant Dose by Sex $[F(3,190) = 8.90, p < .005]$ and Illumination by Dose by Sex $[F(3,190) = 2.75, p < .05]$ interactions. These results showed that detection rates were higher in the light than in the dark for all animals, with the drug producing a larger decrement in detection rate in the light than in the dark, particularly in the males. Detection rate also declined significantly across intervals within the vigilance session $[F(3,190) = 2.71, p < .05]$. However, intervals did not significantly interact with any other variable.

The methylphenidate analysis did not reveal any significant drug effect $[F(3,190) = .44, p < .25]$. However, detection rates were higher in the light than in the dark $[F(1,190) = 8.10, p < .01]$ and were found to decrease significantly with elapsed time $[F(3,190) = 2.71, p < .05]$. There was also significant Replication by Sex interaction $[F(2,190) = 7.54, p < .01]$ present, with the males detecting fewer stimuli during the first replication than in subsequent replications.

Analysis of the false alarm data collected under each drug condition showed that d-amphetamine was the only factor that had a significant effect on false alarms. The drug produced a dose-related reduction in the false alarm rate $[F(3,14) = 11.64, p < .005]$.

when .5 mg/kg or more of methylphenidate is administered subcutaneously to rhesus monkeys (Davis, 1957) and when .4 mg/kg is administered intraperitoneally to rats (Kallman & Isaac, 1975). However, Goethe and Isaac (1977) were unable to find a methylphenidate effect on fixed-interval responding when the drug was administered orally to squirrel monkeys at doses as high as 3.2 mg/kg. These data suggest that the route of administration may be a factor in the effectiveness of the drug on behavior. Another factor that could have contributed to the lack of methylphenidate effect in this study is age. Kallman and Isaac (1975) found an age difference in the responses of albino rats to three different drugs, including methylphenidate. In the monkey studies cited above, Davis (1957) used adult rhesus macaques as subjects, and Goethe and Isaac (1977) used squirrel monkeys of approximately the same age as the subjects used in the present study. These data suggest that factors such as route of administration and age may influence the potency of methylphenidate on behavior.

REFERENCES

ALEXANDER, M., & ISAAC, W. Effect of illumination and d-amphetamine on the activity of the rhesus monkey. *Psychological Reports*, 1965, 16, 311-313.

BARKLEY, R. A. A review of stimulant drug research with hyperactive children. *Journal of Child Psychology and Psychiatry*, 1977, 18, 137-165.

BRADLEY, P. B., & KEY, B. J. The effect of drugs on arousal responses produced by electrical stimulation of the reticular formation of the brain. *Electroencephalography and Clinical Neurophysiology*, 1958, 10, 97-110.

DAVENPORT, W. G. Vigilance and arousal: Effects of different types of background stimulation. *Journal of Psychology*, 1972, 82, 339-346.

DAVIES, D. R., & HOCKEY, G. R. J. The effects of noise and doubling the signal frequency on individual differences in visual vigilance performance. *British Journal of Psychology*, 1966, 57, 381-389.

DAVIS, G. D. Effects of central excitant and depressant drugs on locomotor activity. *American Journal of Physiology*, 1957, 188, 619-623.

DELAY, E. R., GOLDEN, A. J., & STEINER, N. O. A compact IC tone generator. *Physiology & Behavior*, 1978, 21, 133-134.

DELAY, E. R., SMITH, E. S., & ISAAC, W. Effects of illumination on auditory threshold. *Physiology & Behavior*, 1978, 20, 201-202.

DELAY, E. R., STEINER, N. O., & ISAAC, W. Effects of d-amphetamine and methylphenidate upon auditory threshold in the squirrel monkey. *Pharmacology, Biochemistry and Behavior*, 1979, 10, 861-864.

FRANKMANN, J. P., & ADAMS, J. A. Theories of vigilance. *Psychological Bulletin*, 1962, 59, 257-272.

GOETHE, K. E., & ISAAC, W. Effects of amphetamine and methylphenidate on fixed interval responding in the squirrel monkey. *Pharmacology, Biochemistry and Behavior*, 1977, 7, 79-82.

GOODMAN, L. S., & GILMAN, A. *The pharmacological basis of therapeutics*. New York: Macmillan, 1975.

HEBB, D. O. Drives and the C.N.S. (conceptual nervous system). *Psychological Review*, 1955, 62, 243-254.

HINK, R. F., FENTON, W. H., TINKLENBERG, A. P., & KOPELL, B. S. Vigilance and human attention under conditions of methylphenidate and secobarbital intoxication: An assessment using

brain potentials. *Psychophysiology*, 1978, 15, 116-125.

HORNBUCKLE, P. A. Delayed-response performance as a function of sensory stimulation in the squirrel and owl monkey. *Journal of Comparative and Physiological Psychology*, 1972, 79, 99-104.

ISAAC, W. The influence of illumination upon the temporal patterning of responses in squirrel and owl monkeys. *Psychonomic Science*, 1969, 14, 243-244.

ISAAC, W., & DEVITO, J. L. Effect of sensory stimulation on the activity of normal and prefrontal-lobectomized monkeys. *Journal of Comparative and Physiological Psychology*, 1958, 51, 172-174.

ISAAC, W., & TROELSTRUP, R. Opposite effects of illumination and d-amphetamine upon activity in the squirrel monkey *(Saimiri)* and the owl monkey *(Aotes)*. *Psychopharmacologia*, 1969, 15, 260-264.

KALLMAN, W. M., & ISAAC, W. The effects of age and illumination on the dose-response curves for three stimulants. *Psychopharmacologia*, 1975, 40, 313-318.

KALLMAN, W. M., & ISAAC, W. Altering arousal in humans by varying ambient sensory conditions. *Perceptual and Motor Skills*, 1977, 44, 19-22.

KIRK, R. E., & HECHT, E. Maintenance of vigilance by programmed noise. *Perceptual and Motor Skills*, 1963, 16, 553-560.

LINDSLEY, D. B. Attention, consciousness, sleep and wakefulness. In J. Field, H. W. Magoun, & V. E. Hall (Eds.), *Handbook of physiology: Neurophysiology* (Vol. III). Washington, D.C: American Physiological Society, 1960.

LOEB, M., HAWKES, G. R., EVANS, W. O., & ALLUISI, E. A. The influence of d-amphetamine, benactyzine and chlorpromazine on performance in an auditory vigilance task. *Psychonomic Science*, 1965, 3, 29-30.

LOWTHER, W. R., & ISAAC, W. The effects of d-amphetamine and illumination on behaviors of the squirrel monkey. *Psychopharmacology*, 1976, 50, 231-235.

MACKWORTH, J. F. The effect of amphetamine on the detectability of signals in a vigilance task. *Canadian Journal of Psychology*, 1965, 19, 104-110.

MACKWORTH, N. H. Some factors affecting vigilance. *The Advancement of Science*, 1957, 53, 389-393.

McGRATH, J. J. Irrelevant stimulation and vigilance performance. In D. N. Buckner & J. J. McGrath (Eds.), *Vigilance: A symposium*. San Francisco: McGraw-Hill, 1963.

SCOTT, W. E., JR. Activation theory and task design. *Organizational Behavior and Human Performance*, 1966, 1, 3-30.

SEEGAL, R. F., & ISAAC, W. Sensory influences upon amphetamine tolerance. *Physiology & Behavior*, 1971, 7, 877-879.

STARZL, T. E., TAYLOR, C. W., & MAGOUN, H. W. Collateral afferent excitation of reticular formation of brain stem. *Journal of Neurophysiology*, 1951, 14, 479-496.

STINNETTE, M. J., & ISAAC, W. Behavioral effects of d-amphetamine and caffeine in squirrel monkeys. *European Journal of Pharmacology*, 1975, 30, 268-271.

STROH, C. M. *Vigilance: The problem of sustained attention.* Oxford: Pergamon Press, 1971.

WATKINS, W. H., & FEEHRER, C. E. Acoustic facilitation of visual detection. *Journal of Experimental Psychology*, 1965, 70, 332-333.

WERRY, J. S. Medication for hyperkinetic children. *Drugs*, 1976, 11, 81-89.

WHALEN, C. K., & HENKER, B. Psychostimulants and children: A review and analysis. *Psychological Bulletin*, 1976, 83, 1113-1130.