Pharmacology Biochemistry & Behavior, Vol 24, pp 503–506, 1986 © Ankho International Inc Printed in the U S A 0091-3057/86 $3 00 + 00

Effects of Drugs, Age and Illumination on Response Speed of Squirrel Monkeys[1]

NICOLE O. STEINER,[2] EUGENE R. DELAY[3] AND WALTER ISAAC

Department of Psychology, University of Georgia, Athens, GA

Received 7 May 1985

STEINER, N O , E R DELAY AND W ISAAC *Effects of drugs, age and illumination on response speed of squirrel monkeys* PHARMACOL BIOCHEM BEHAV **24**(3) 503–506, 1986 —Four young (2½ years) and four older (over 10 years) squirrel monkeys were used to study age differences in the effects of d-amphetamine, methylphenidate and illumination on response speed Although young monkeys were faster than the old monkeys, only the older monkeys showed an illumination effect Both d-amphetamine and methylphenidate slowed response speed but only in the older monkeys and only when illumination was present These results suggest that older, mature squirrel monkeys are more sensitive to the effects of d-amphetamine, methylphenidate and illumination than young squirrel monkeys

Amphetamine Methylphenidate Age Illumination Squirrel monkey Response speed

PREVIOUS studies have suggested that the presence of ambient illumination facilitates behavior of diurnal animals on measures such as reaction time, fixed interval responding and locomotor activity, while in nocturnal animals the presence of ambient light results in response decrements on these measures [1, 6, 12, 14, 16, 17] Ambient illumination has been found to alter cortical activity in the rat, changes which correlated with illumination induced changes in behavior [18] Studies have also shown that the level of ambient light, as well as the age of the organism, will influence the effects of dextroamphetamine sulfate and methylphenidate hydrochloride on behavior Kallman and Isaac [17] found that young rats displayed a greater illumination dependent locomotor activity response than older rats and, while all rats exhibited a greater dose related increase in activity in the light than in the dark, the young rats were more responsive to d-amphetamine at low doses and older rats were more responsive to the drug at higher doses Although d-amphetamine has been classified as a central nervous system stimulant [10], not all organisms respond to this drug as a behavioral stimulant Studies with diurnal primates have suggested that d-amphetamine acts as a behavioral depressant on fixed interval responding [9], locomotor activity [1, 3, 16, 19], vigilance performance [5] and auditory thresholds [7], an effect most pronounced in the presence of ambient light [5,16] One of the hypothesized effects of d-amphetamine is that it reduces the influence of illumination on behavior [1] One study [19] using infrared closed circuit television to observe adult squirrel monkeys, found that d-amphetamine reduced the frequencies of behavioral patterns occurring predominantly in the light while increasing those behaviors normally seen in the dark Since the effects of illumination have been found to vary with age, it might be expected that the effects of d-amphetamine would thus be modified by age differences of the subjects studied As yet, however, age related differences in responding to illumination and d-amphetamine have not been examined in diurnal primates

Methylphenidate has also been found to interact with the effects of illumination, producing greater increases in locomotor activity in the light than in the dark [17] Again, Kallman and Isaac [17] found young rats more sensitive to higher doses of the drug However, a lack of effect has been reported for young squirrel monkeys on behavioral measures such as auditory thresholds [7], fixed-interval responding [9] and locomotor activity [15] On the other hand, pacing behavior of adult rhesus monkeys has been reported to be reduced by methylphenidate [3] These studies suggest potential age differences in the response of diurnal primates to methylphenidate

The present study attempted to examine differences in responding of young and old squirrel monkeys to d-amphetamine, methylphenidate and ambient illumination with a task involving a discrete motor response

METHOD

Subjects

Four squirrel monkeys (*Saimiri sciureus*), in each of two age groups served as subjects The young monkeys were 2½ years of age and the older monkeys were over 10 years, having been received in the laboratory as young adults approximately 10 years before the present study, making the latter group at least middle aged for this species [2] All

[1]This research was supported in part by Research Grant MH 25164 from the National Institute of Mental Health

[2]Nicole O Steiner is now in Bogata, Colombia

[3]Requests for reprints should be addressed to Dr Eugene R Delay, Department of Psychology, Regis College, W 50th and Lowell Blvd , Denver, CO 80221

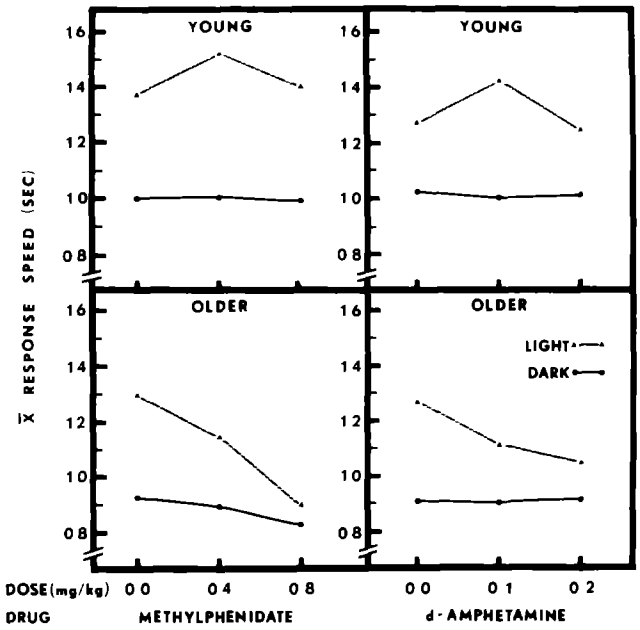

FIG 1 The mean response speeds (1/X) of the young ($2^1/_2$ years) and older (over 10 years) squirrel monkeys tested under light and dark sensory conditions and with three doses of d-amphetamine and three doses of methylphenidate

animals had served in previous experiments using d-amphetamine and methylphenidate The animals were housed in a colony maintained on a 12 hr light-12 hr dark cycle (light on at 5 a m) The animals had free access to water while in the colony and food was available after each test session Weights, taken every 6 days, remained within normal limits compared to the other monkeys in the colony Each animal was tested at the same time each day with all animals tested between 1 and 4 p m

Apparatus

The animals were transported and tested in an expanded metal carrying cage 24×24×38 cm long Black Plexiglas doors enclosed both ends of the transport cage A translucent Plexiglas lever (Davis, Model BD-2), inserted through a small opening in one door, served both as a response manipulandum and as the reinforcement site The lever was illuminated internally with a dim light throughout the test sessions under both illumination conditions used The transport cage was placed in a sound attenuated chamber, measuring 71×71×53 cm high and painted flat white inside The door of the chamber had a 28×43 cm Thermopane observation window covered with cheese cloth on the outside Illumination within the cage measured 376 75 lx when a fluorescent light mounted on chamber ceiling was on and less than 10 76 lx when the light was off A ventilation fan provided 68 dB masking noise (C scale, re. 20 $\mu N/m^2$) The auditory stimulus was a 4 kHz tone generated by solid state circuitry [4] and delivered through an 8 ohm speaker to the inside of the chamber 45 cm from the center of the transport cage The sound pressure level of the stimulus was 8–10 dB above each monkey's threshold in the light [7] All programming and recording equipment was located in a separate room

Procedures

Short reaction times were selectively reinforced with sweetened Hawaiian Punch delivered through the response lever by varying the duration of stimulus presentations and reinforcing only those responses made while the stimulus was on Each of the five stimulus durations (0 3, 0 7, 1 1 1 5 and 1 9 sec) was presented 5 times during a test session for a total of 25 trials per session, ordered according to a latin square design with a different latin square used for each test session Three warmup trials in which the stimulus duration and required response latency was 1 9 sec were given each day before the actual testing and data collection began Reaction times of 10 sec or less were recorded on every trial, all response latencies exceeding 10 sec were recorded as failures to respond The monkeys were trained until they reached a criterion of 8 or more reinforcers during a test session, both in the light and in the dark The intertrial intervals were 30, 50, 70, 90 and 110 sec, presented according to a latin square design The monkeys were tested under ambient light and dark conditions which were alternated, one day light and one day dark, throughout the experiment Half of the monkeys (1 male and 1 female from each age group) began the experiment with a test session in the light and the others began with a session in the dark

Drug presentation was counterbalanced with 1 male and 1 female from each age group beginning the experiment with a series of three replications with one drug and then, after a 5-day period during which the experimental procedures were continued but with no drug given, with a second series of three replications with the second drug That is, 4 monkeys began the experiment with methylphenidate and ended with d-amphetamine while the other 4 monkeys began the experiment with methylphenidate and ended with d-amphetamine The daily doses of placebo (bacteriostatic water), 2 doses (0 1 and 0 2 mg/kg body weight) of d-amphetamine (Smith, Kline & French) and 2 doses (0 4 and 0 8 mg/kg body weight) of methylphenidate (Ciba Geigy) were each mixed in 9 cc of sweetened Hawaiian Punch These doses were selected to avoid potentially confounding the experimental outcome by altering auditory thresholds [7] The assigned dose was administered orally after the subject entered the carrying cage The test session began 15 min after drug administration A replication consisted of one day for each drug level under each illumination condition, for a total of 6 days per replication The sequence of drug doses for each monkey was assigned using a latin square design and a different sequence of doses was used for each illumination condition in each replication The first replication under each drug served to adapt the monkeys to the taste of the drug in the punch solution, so that they would reliably accept the drug, and to any changes in internal stimulus conditions related to the nonspecific effects of the drugs Data from the last two replications with each drug were evaluated with analysis of variance

RESULTS

The reaction times in each test session were transformed to the reciprocal as recommended [8] for timed measures and an analysis of variance was performed on the sum of the 5 fastest response times in each session [13] The data for the last two replications under each drug condition were pooled

and analysed to examine the effects of age (2), sex (2), illumination (2), drug (2) and dose (3) The analysis indicated that age, $F(1,4)=9\ 04$, $p<0\ 05$, sex, $F(1,4)=24\ 09$, $p<0\ 01$, illumination, $F(1,4)=27\ 52$, $p<0\ 01$, and dose, $F(2,8)=5\ 42$, $p<0\ 05$, all produced significant differences in response speed In summary, the younger monkeys responded faster than the older monkeys, females were faster than males, response times were shorter in the light and the responses were slowed by increasing doses of the drugs The analysis also revealed significant interactions of dose by age, $F(2,8)=10\ 83$, $p<0\ 01$, dose by illumination, $F(2,8)=17\ 15$, $p<0\ 01$, and dose by age by illumination, $F(2,8)=42\ 53$, $p<0\ 01$, limiting the generality of the findings Inspection of these data (Fig 1) indicated that these effects were generated primarily by the older monkeys, they exhibited greater dose related decrements in response speed than the young monkeys, primarily when ambient light was present The drug factor did not produce a significant main effect nor interact significantly with any other variable

Because of the significant interactions between age and other variables, as well as to allow the identification of further age related effects upon response speed, a separate analysis examining the effects of sex (2), illumination (2), drug (2), and dose (3) was performed on the data obtained for each age group The analysis of the older monkeys' response speeds indicated that responding was faster in the light than in the dark, $F(1,2)=29\ 00$, $p<0\ 05$, and that females responded more quickly than males, $F(1,2)=20\ 66$, $p<0\ 05$ This analysis also revealed a significant slowing of response speeds with increasing drug dose, $F(2,4)=15\ 24$, $p<0\ 05$ Furthermore, a significant illumination by dose interaction, $F(2,4)=7\ 34$, $p<0\ 05$, indicated that the dose related decrement in response speed occurred primarily in the light Again, however, no significant differences between the effects of d-amphetamine and methylphenidate were found in the response speeds of the older animals The analysis of the response speeds of the young animals indicated that none of the variables examined had a significant effect on responding

DISCUSSION

In agreement with earlier studies investigating reaction times in diurnal primates [12], the present study found that reaction times of squirrel monkeys were faster in the light than in the dark Although it was found that younger monkeys gave faster responses than the older monkeys, the separate analyses for the two age groups showed only a significant illumination effect in the older animals A similar observation has been made in the rat [6] This suggests that while the arousal level of the younger monkeys is higher than that of the older monkeys, it is less dependent upon environmental stimuli for its maintenance

The absence of a drug effect in the younger monkeys was unexpected However, other investigators [11] have found that d-amphetamine is metabolized at a faster rate in the brain of young animals than in older animals Such a finding would suggest an age difference in the dose effectiveness of the drug, and while the dose levels of d-amphetamine used in the present study have been found to be effective in young monkeys on a variety of behaviors [5, 7, 9, 16] and to be interactive with the level of ambient light [5,16], they were too low to produce changes in the response used in the present study Moreover, while methylphenidate has been found to be ineffective in young squirrel monkeys [5, 7, 9] even with doses four times those used in this study [15], the drug has been reported to reduce pacing activity in the adult rhesus monkey [3] These data, along with the present findings, suggest a greater sensitivity to these drugs in the older subjects, with the response to both drugs being dependent upon the level of ambient light

Since the subjects studied in earlier work reported from this laboratory were young squirrel monkeys, the observation of the reduced effectiveness of these drugs in young squirrel monkeys reconciles earlier findings suggesting that methylphenidate had no observable effect upon the behaviors studied with the findings of others While the dose effectiveness of the two drugs differs, both drugs appear to act in a similar fashion and the effects of both are dependent upon ambient illumination

REFERENCES

1 Alexander, M and W Isaac Effect of illumination and d-amphetamine on the activity of the rhesus monkey *Psychol Rep* **16**: 311–313, 1965

2 Bowden, D M and M L Jones Aging research in nonhuman primates In *Aging in Nonhuman Primates*, edited by D M Bowden New York Van Nostrand Reinhold Company, 1979

3 Davis, G D Effects of central excitant and depressant drugs on locomotor activity in the monkey *Am J Physiol* **188**: 619–623, 1957

4 Delay, E R , A J Golden and N O Steiner A compact IC tone generator *Physiol Behav* **21**: 133–134, 1978

5 Delay, E R and W Isaac The effects of illumination, d-amphetamine, and methylphenidate upon vigilance performance of squirrel monkeys *Bull Psychonom Soc* **15**. 203–206, 1980

6 Delay E R and W Isaac Age and arousal in the rat *Bull Psychonom Soc* **21**· 294–296, 1983

7 Delay, E R , N O Steiner and W Isaac Effects of d-amphetamine and methylphenidate upon auditory threshold in the squirrel monkey *Pharmacol Biochem Behav* **10**: 861–864, 1979

8 Edwards, A L *Experimental Design in Psychological Research* New York Rinehart, 1972, p 107

9 Goethe, K E and W Isaac Effects of amphetamine and methylphenidate on fixed interval responding in the squirrel monkey *Pharmacol Biochem Behav* **7**. 79–82, 1977

10 Goodman, L S and A Gilman *The Pharmacological Basis of Therapeutics* New York MacMillan Co , 1975, p 496

11 Honecker, H and H Coper Kinetics and metabolism of amphetamine in the brain of rats of different ages *Arch Pharmacol* **291**: 111–121, 1975

12 Hornbuckle, P A Delayed-response performance as a function of sensory stimulation in the squirrel and owl monkey *J Comp Physiol Psychol* **79**: 99–104, 1972

13 Isaac, W Arousal and reaction times in cats *J Comp Physiol Psychol* **53**: 234–236, 1960

14 Isaac, W The influence of illumination upon the temporal patterning of responses in squirrel and owl monkeys *Psychonom Sci* **14**: 243–244, 1969

15 Isaac, W and M D Kallman Locomotor effects of d-amphetamine and methylphenidate in young squirrel monkeys *Bull Psychonom Soc* **14**: 315–317, 1979

16 Isaac, W and R Troelstrup Opposite effect of illumination and d-amphetamine upon activity in the squirrel monkey (Saimiri) and owl monkey (Aotes) *Psychopharmacologia* **15** 260–264 1969

17 Kallman, W M and W Isaac The effects of age and illumination on the dose-response curves for three stimulants *Psychopharmacologia* **40:** 313–318, 1975

18 Lorig, T S and W Isaac Quantification of cortical arousal correlation with locomotor activity *Physiol Psychol* **12** 253–256, 1984

19 Lowther, W R and W Isaac The effects of d-amphetamine and illumination on behaviors of the squirrel monkey *Psychopharmacology (Berlin)* **50** 231–235 1976