A COMPARISON OF TWO STIMULANTS ON THE VIGILANCE PERFORMANCE OF RATS

DENISE LYNN SQUIRE

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An Abstract

Presented to the

Graduate and Research Council of

Austin Peay State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Arts

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by

Denise Lynn Squire

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ABSTRACT

Centrally acting drugs have been demonstrated to alter cortical arousal. Both cocaine and d-amphetamine are classified as stimulants and have been found to produce similar effects on both cortical and behavioral arousal as measured by the EEG and locomotor activity. Discrimination studies which report that, subjectively, animals treat the two drugs as equivalent have further strengthened this similarity. However, some discrepancies have been found in this model. Cocaine and d-amphetamine produce dissimilar types of locomotor activity depending on the familiarity of the environment. In addition, it is believed that cocaine and d-amphetamine affect the neurotransmitters dopamine and norepinephrine differently. The present study further compares cocaine and d-amphetamine using a more sensitive measure.

Twenty-four rats, approximately 217 days of age, served in one of two gender balanced groups. Prior to each testing session, the rats received one of three dosages of d-amphetamine (0.0, 0.2, 0.4 mg/kg) or cocaine (0.0, 1.0, 2.0 mg/kg). The rats were then tested on an auditory vigilance task. A total of 6 replications were conducted.

The results indicate a difference in the two drugs in both the detection rate and the false alarm rate. Male rats, when injected with cocaine, showed an increase in

detection rate with increasing dosages. Female rats on cocaine and all animals on d-amphetamine only showed an increase in overall responding. These findings suggest that cocaine increases the attention of male rats, while d-amphetamine simply increases the overall response rate.

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Denise Lynn Squire

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To the Graduate and Research Council:

I am submitting herewith a Thesis written by Denise Lynn Squire entitled "A Comparison of Two Stimulants on the Vigilance Performance of Rats." I have examined the final copy of this paper for form and content, and I recommend that it be accepted in partial fulfillment of the requirements for the degree Master of Arts with a major in Psychology.

Major Professor

We have read this thesis and recommend its acceptance:

Second Committee Member

Third Committee Member

Accepted for the Graduate and Research Council:

Dean of the Graduate School

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CHAPTER 1

Review of the Literature

Introduction

Stimulant drugs tend to be widely abused in our society. Behaviorally, these drugs are associated with increases in arousal, gross locomotor activity, and alerting. However, because the category of stimulants is so broad, it contains a number of drugs which produce different effects and attain varying degrees of popularity within society. Amphetamine was widely abused in the 1960's and 1970's, while in the 1980's cocaine frequently appears to be the drug of choice. The present study addresses both similarities and differences between these two stimulants, particularly as they alter arousal and attention as measured by an auditory vigilance task.

Arousal

The phenomenon of cortical arousal typically has been measured by the use of electroencephalography. In the aroused state, the cortical electroencephalogram (EEG) has a desynchronized pattern with low amplitude and high frequency. This is in contrast to the "drowsy" cortical EEG pattern of synchronous high amplitude, low frequency waves. Starzl, Taylor, and Magoun (1951a) reported that electrical stimulation of the brainstem reticular formation

produced desynchronized electrical activity of the cerebral cortex which resembled that of the arousal reaction. Starzl et al. (1951b) observed that pain producing stimulation of the sciatic nerve and the noise made by a toy cricket would also produce the electrical pattern associated with alerting. This latter demonstration confirmed the idea that in addition to direct electrical stimulation, sensory stimulation can also lead to cortical arousal. These studies, however, do not address themselves to behavioral arousal since they used paralyzed animals and acute preparations.

Subsequent research (Segundo, Arana, & French, 1955) found that when direct stimulation was applied to the reticular formation, non-paralyzed monkeys would raise their heads, retract their ears and appear to become alert. This same stimulation also produced a desynchronized EEG. These researchers were able to demonstrate a relationship between cortical and behavioral arousal and that both appear to be mediated by the brainstem reticular formation.

Another idea associated with the concept of arousal is that increased arousal will be associated with improved performance. Stimulation to the brainstem of monkeys was found to increase the animals' ability to perform a discrimination task (Fuster, 1958). Isaac (1960) found that sensory stimulation produced the same reduction in the motor reaction times of cats as electrical stimulation of

the reticular formation. Surwillo (1969), by measuring EEG activation, also demonstrated the association between arousal and performance. Stennett (1957) demonstrated this relationship but found that it is not necessarily linear. He reported that performance improved with increasing arousal only to a point beyond which performance started to deteriorate as arousal continued to increase. This phenomenon is often referred to as an inverted-U shaped relationship between level of arousal and performance.

Once the ability of sensory stimulation to alter arousal levels had been established, a number of additional studies were conducted to further investigate the relationship in both human and non-human species. Illumination has been found to increase arousal in diurnal animals as measured by increased locomotor activity in monkeys (Isaac & Devito, 1958) and increased detection rates in both monkeys and humans on a vigilance task (Chavez & Delay, 1982; Delay & Isaac, 1980). Kallman and Isaac (1977) reported a reduction in the reaction times of humans tested in the light when compared to the dark. Although illumination also alters arousal level in rats, a nocturnal species, the direction of the effect typically is opposite to that reported for diurnal organisms. These studies linking the behavioral measures of motor reaction time, activity, and vigilance to sensory stimulation induced alterations in arousal suggest that they may also

serve to measure the effects of other types of manipulation, such as centrally acting drugs, upon arousal.

Stimulant Drugs

Both d-amphetamine sulfate and cocaine hydrochloride are classified as stimulant drugs (DiPalma, 1971). It has been found that when amphetamine is injected into cats, it produces cortical arousal as reflected by an EEG of low amplitude and fast activity (Bradley, 1958). Bradley also reported that the amphetamine caused behavioral alerting and hyperactivity in the cats. Similar increases in activity have been observed in rats injected with d-amphetamine (Kallman & Isaac, 1975; Seegal & Isaac, 1971). Wood and Golden (1987) found that cocaine produced an illumination dependent dosage related increase in the locomotor activity of rats similar to that reported by Kallman and Isaac for d-amphetamine. Under the influence of higher dosages of both d-amphetamine and cocaine, cats tend to exhibit stereotyped behavior consisting of head and eye movements along with a desynchronized EEG (Wallach & Gershon, 1971). d-Amphetamine and cocaine seem to produce similar alterations in cortical EEG and to have parallel behavioral effects on locomotor activity and stereotypy in several species of animal.

Many operant discrimination studies have reported that animals, trained to press one lever when injected with

saline and another when injected with amphetamine, will respond on the amphetamine lever following an injection of cocaine (Castellano, 1974; Colpaert, Niemegeers, & Janssen, 1978; D'Mello & Stolerman, 1977; Jarbe, 1978). The response learned while under the influence of one drug is generalized to the other suggesting that, from the organism's point of view, cocaine and amphetamine have similar effects.

Even though most of the literature points out similarities between the two drugs, there are some documented differences. d-Amphetamine, which typically increases the locomotor activity of rats, has been reported to produce a decrease in locomotor activity when the rats are placed into a novel environment (Miller, Sethna, & Young, 1970). This effect of the testing environment is opposite to that reported for cocaine. Following injections of cocaine, rats mainly produce an alerting reaction in a familiar environment, but when placed in a novel environment they exhibit high levels of intense locomotor activity (Scheel-Kruger, Braestrup, Nielson, Golembiowska, & Mogilnicka, 1977). It has also been suggested by Jarbe (1978) that, even though the two drugs are similar enough to produce generalization to one another in discrimination tasks, the subjective experience may be different. These findings suggest that there might be additional differences between d-amphetamine and cocaine to

which the more commonly used behavioral measures are not sensitive.

Neurotransmitters

Important to any discussion of centrally acting drugs is the neurochemical basis by which they operate. It is believed that both cocaine and d-amphetamine interact with the two major monoaminergic neurotransmitters dopamine and norepinephrine. Scheel-Kruger (1972) suggests that both drugs cause a decrease in the overall norepinephrine content of the brain while increasing the rate of norepinephrine metabolism. Of the two drugs, only d-amphetamine seems to increase the rate of dopamine metabolism (Scheel-Kruger). It also has been suggested that d-amphetamine acts directly as a mimicker of dopamine and norepinephrine at the synapse (Van Rossum, 1970; Van Rossum, Van Der Schoot, & Hurkmans, 1962). Cocaine, on the other hand, tends to produce its effects by forcing a release of endogenously available norepinephrine and dopamine (Van Rossum et al.).

This difference in neurotransmitter related effects of cocaine and d-amphetamine becomes evident when the drugs α-methyltyrosine and reserpine are used as pretreatments. Both α-methyltyrosine and reserpine act mostly on norepinephrine with some dopamine involvement, but do so using different aspects of the neurotransmitters.

α-Methyltyrosine blocks the synthesis of dopamine and norepinephrine without altering the existing stores of these neurotransmitters. Reserpine effects these neurotransmitters by depleting the existing stores without blocking their metabolism (Goldberg & Salama, 1970; Scheel-Kruger et al., 1977). Because of this, different responses to d-amphetamine and cocaine are found following retreatment with α-methyltyrosine or reserpine. When using reserpine, the d-amphetamine effects are not altered but the cocaine effects are eliminated (Van Rossum et al, 1962). α-Methyltyrosine, however, does not eliminate the cocaine effect (Scheel-Kruger et al., 1977). It further was found that when reserpine treated rats are given L-DOPA, a precursor of dopamine, the previously eliminated cocaine response is restored (Van Rossum et al.). Substantia nigra lesions produced by the neurotoxin 6-hydroxydopamine (6-OHDA), which markedly reduce both the amount of dopamine in the brain and the rate of its synthesis, block the response to both cocaine and d-amphetamine (Creese & Iversen, 1975). These findings suggest that cocaine is dependent upon existing pools of dopamine and norepinephrine while d-amphetamine is more dependent upon the ability of the brain to synthesize fresh supplies of these neurotransmitters.

Other differences between the neurochemical effects of cocaine and d-amphetamine also have been reported.

Scheel-Kruger et al. (1977) have suggested that d-amphetamine stimulates the synaptic release of norepinephrine and dopamine with only slight blockage of pre-synaptic reuptake, while cocaine mostly blocks the reuptake but has little releasing ability. Because of these neurochemical effects, cocaine has been compared more often to the anti-Parkinsonian drug benztropine (Cogentin) and the tricyclic antidepressant imipramine (Tofranil) than to d-amphetamine.

While the impact of these various neurochemical differences on behavior are not well understood at this time, they do support the suggestion that the differences in the behavioral effects of cocaine and d-amphetamine, although probably subtle, should be more evident than is currently indicated by the literature.

Gender Differences

Gender differences, both neurochemical and behavioral, have been documented in the rat. When chronically pretreated with α-methyltyrosine, a norepinephrine depleting drug, male and female rats exhibited different recovery rates when tested 12 hours after termination of the treatment (Gordon & Shellenberger, 1974). Female rats recovered about 47% of the depleted norepinephrine, while male rats only recovered 20%. Other studies that investigated the effects of estrogen on dopamine related

behaviors also found differing results depending on the gender of the animal (Gordon, Borison, & Diamond, 1980; Hruska & Silbergeld, 1980). Stereotypy, induced by amphetamine, was increased in male rats pretreated with estrogen, but the stereotypy was reduced in female rats. These studies suggest that there might be gender related neurochemical differences which have not yet been investigated fully.

Vigilance

Vigilance performance consists of attending to a brief stimulus which serves as a discriminative cue for an operant response. Goodman (1970) found that whenever monkeys were attending to the stimulus and made a correct response, the multiple-unit activity of the mesencephalic reticular formation fell within a restricted frequency range. It was also demonstrated by Fuster (1958) that induced arousal caused by stimulating the core of the brainstem at the level of the mesencephalon increased the monkeys' ability to perform a discrimination task. Both Fuster and Goodman demonstrated the electrophysiological relationship between mesencephalic activation and improved performance on tasks requiring attention.

Other arousal altering variables also have been shown to improve vigilance performance. Chavez and Delay (1982) demonstrated this phenomenon of increased attention by elevating arousal using ambient illumination on humans. Centrally acting stimulants, such as d-amphetamine which have been found to increase arousal, have also been found to alter vigilance performance (Delay & Isaac, 1980). It is evident from these findings that, whether arousal is produced by stimulation of the brainstem, sensory stimulation, or by centrally acting drugs, arousal produces increased attention.

Summary

Changes in arousal have always been associated with centrally acting drugs such as cocaine and d-amphetamine. Since both drugs are classified as stimulants, gross behavioral measures, such as locomotor activity, have shown similar effects for the two. More recent studies however, have found that, even though both drugs increase gross locomotor activity, they do so differently. Further evidence shows that cocaine and d-amphetamine operate on different aspects of the same neurotransmitters, norepinephrine and dopamine, and that the responsiveness of these neurotransmitters is different in males and females. It is apparent that a more sensitive measure of arousal is needed to further investigate these differing qualities.

The present study investigates the different behavioral effects of cocaine and d-amphetamine on vigilance performance.

CHAPTER 2

Method

Subjects

Twenty-four CD derived albino rats, born at Austin Peay State University, approximately 158 days of age at the start of training and 217 days of age at the start of testing, served in one of two gender balanced groups. The rats were housed individually with food (Wayne Lab Blox) available ad lib and water available for 10 minutes daily beginning one hour after testing. A LD 12:12 lighting schedule (lights on 6 am to 6 pm CST) was maintained throughout training and testing. The mean weights recorded prior to the first day of testing were 410 g for the male cocaine animals, 227 g for the female cocaine animals, 379 g for the male d-amphetamine animals, and 229 g for the female d-amphetamine animals. At the end of the drug testing the male cocaine animals weighed 428 g, the female cocaine animals were 225 g, the male d-amphetamine animals were 397 g, and the female d-amphetamine animals weighed 235 g.

Apparatus

The rats were tested in 24.7 x 18.0 x 18.0 cm galvanized cages. One end of the cage was wood with a 5.8 cm diameter opening centered 4.0 cm above the mesh

floor. The manipulandum was an acrylic panel located in the opening and hinged at the top, requiring a displacement of approximately .3 cm for detection. The cages were located in sound attenuating cubicles, closed on all sides. Illumination of 765 lx was provided by a 20w fluorescent lamp mounted at the top of each chamber. Ballast transformers for the lights were mounted outside the chambers in order to prevent excessive heat accumulation. The reinforcer was .1 ml of water with the delivery mechanism located immediately to the right of the panel. The stimulus consisted of a 4 kHz tone generated by solid state circuitry similar to that described by Delay, Golden, and Steiner (1978). Tones were presented individually through speakers mounted on the front of each cage and measured 3-4 db SPL (A scale, re: 20 $\mu N/m^2$) above the ambient noise level of 48 db SPL. Trials were presented and data recorded by an Advanced Digital SuperSix computer located in an adjacent room.

Procedure

Training and testing took place between the hours of 7:00 AM and 11:00 AM CST. The rats were trained beginning with a continuous tone. The tone-on period was gradually decreased to 2 seconds. Reinforcement was available only during the tone-on period. Before each tone-on period there was a time-out period such that the tone would not be

presented until a minimum amount of time had elapsed without a response. The duration of the time-out period was gradually lengthened from 1 to 10 seconds during the training period.

Following training, the drug test sessions were conducted only on alternate days. During testing, a tone-off period with a range of 55-157 seconds and a mean of 109.5 seconds was used with a tone-on period of 2 seconds followed by an additional 2 second hold. The 10 second mandatory non-response time-out was employed throughout the drug testing sessions. Each test session consisted of twenty-four trials, resulting in a test session approximately 50 minutes in length.

Prior to each test session, the rats received one of three dosages of d-amphetamine sulfate (Sigma Chemical, 0.0, 0.2, 0.4 mg/kg, measured as the salt) or cocaine hydrochloride (Sigma Chemical, 0.0, 1.0, 2.0 mg/kg, measured as the salt) injected intraperitoneally in an isotonic saline vehicle (1 ml/kg). The selection of equivalent dosages was based upon the report by Colpaert et al. (1978). Half of the rats received the d-amphetamine sulfate and half of the rats received the cocaine hydrochloride. All of the rats in each drug group received all dosages of the assigned drug before repeating a dosage and all dosages were administered 6 times.

CHAPTER 3

Results

The data were transformed to the $\sqrt{X} + \sqrt{X+1}$ as suggested by Edwards (1985) for frequency data and subjected to a mixed design analysis of variance. In order to observe changes within sessions the data from individual trials were collapsed into three blocks of 8 trials each prior to analysis. Differences between individual means were determined using the Studentized Range Test (SRT).

Analysis of the number of reinforcements obtained indicated a significant difference between males and females across the three trial blocks, $F(2, 1060) = 15.02$, $p<.001$.As can be seen in Figure 1, reinforcements earned by the females were relatively consistent, while the reinforcements for the males decreased significantly within sessions, SRT, $\alpha=.01$. A difference in reinforcement responding was also found between cocaine and d-amphetamine within sessions, $F(2, 1060) = 7.54$, $p<.001$, such that cocaine produced a greater number of reinforcements in the first 8 trial block when compared to d-amphetamine and significantly decreased from the first to the third 8 trial block. Reinforcements obtained by the d-amphetamine group remained constant across all three 8 trial blocks, SRT, $\alpha=.01$, (see Figure 2).

Figure 1. Reinforcement Responding for Females and Males Across the Three 8 Trial Blocks.

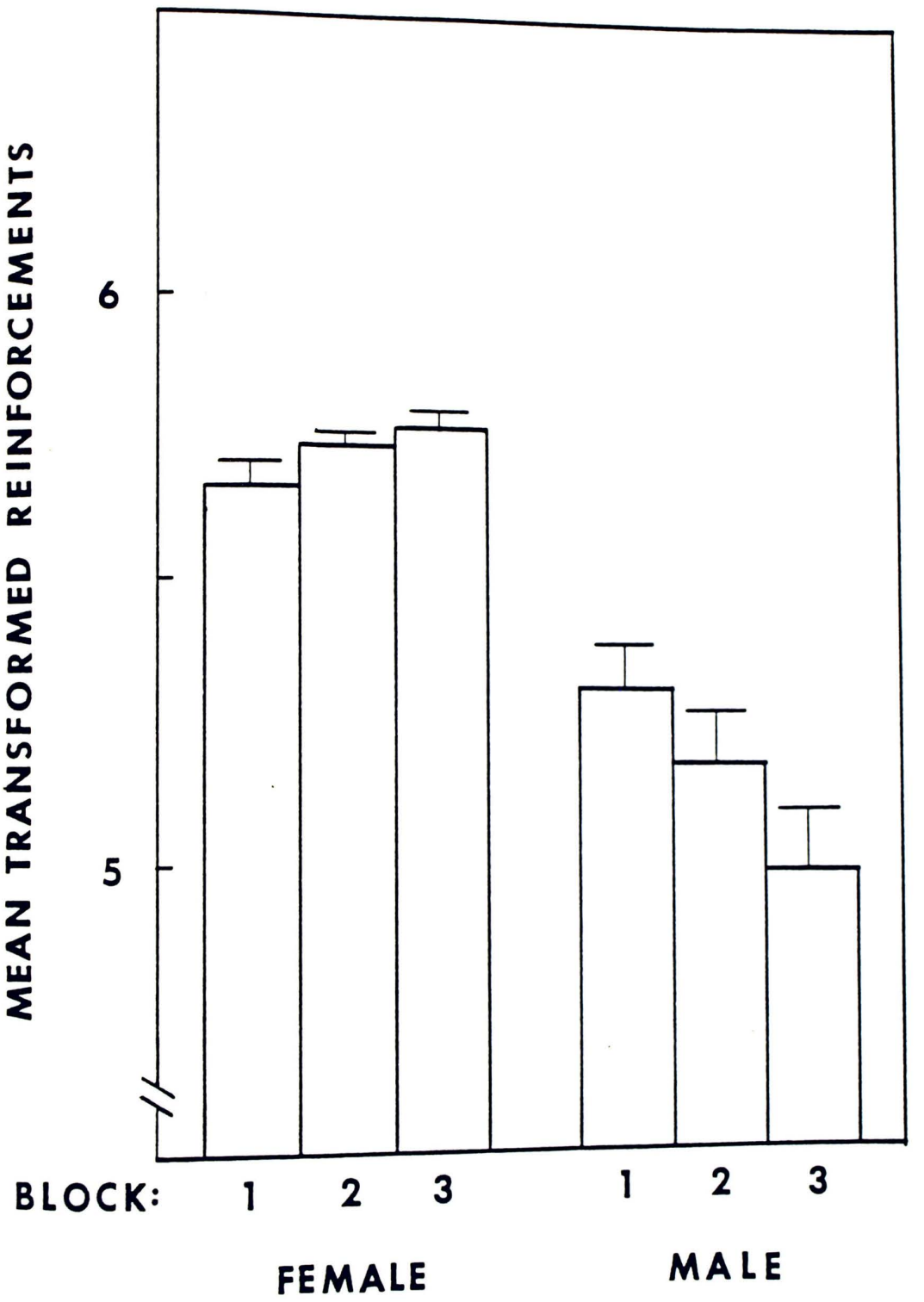
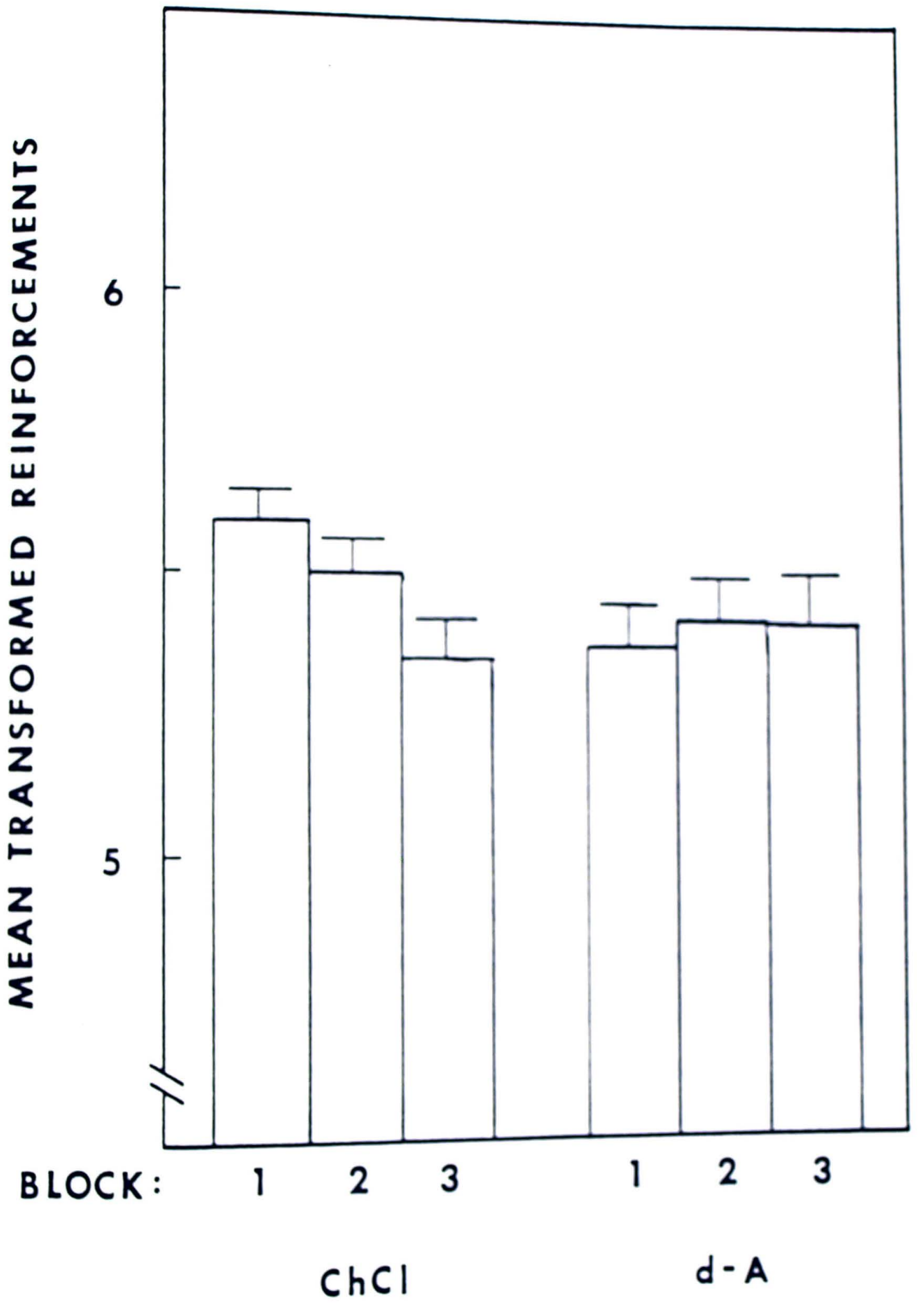

MEAN TRANSFORMED REINFORCEMENTS
6
5
BLOCK:
1
2
3
1
2
3
FEMALE
MALE

Figure 2. Reinforcement Responding Across the Three 8 Trial Blocks for Cocaine (ChCl) and d-Amphetamine (d-A).


MEAN TRANSFORMED REINFORCEMENTS
6
5
BLOCK:
1
2
3
1
2
3
ChCl
d-A

Overall, reinforcements increased with increasing dosage levels, $F(2, 1060) = 10.40$, $p<.001$. This increase was neither independent of gender, $F(2, 1060) = 4.18$, $p<.05$, nor of drug conditions, $F(2, 1060) = 6.52$, $p<.005$. Furthermore, these three variables combined to produce a second order interaction, $F(2, 1060) = 3.96$, $p<.05$. Simple effects analysis indicated that the reinforcements obtained by the males under the influence of cocaine were found to vary significantly across dosages, $F(2, 1060) = 22.93$, $p<.001$. No dose effects were obtained for the males receiving d-amphetamine, $p>.05$, or for the females receiving either drug, $p>.05$, (see Figure 3).

Analysis of the false alarm data revealed that false alarm responding varied significantly across the three 8 trial blocks within sessions, $F(2, 1060) = 124.72$, $p<.001$. False alarms also differed as a function of dosage level, $F(2, 1060) = 14.42$, $p<.001$, although this change was not stable within sessions, $F(4, 1060) = 2.88$, $p<.05$. Further analysis revealed that false alarms under all dosage levels decreased significantly from the first 8 trial block to the second and third 8 trial blocks within sessions, SRT, $\alpha=.01$. A significant increase in false alarms was also found in the second and third 8 trial blocks between placebo and the high dosage level, SRT, $\alpha=.01$ (see Figure 4).

Figure 3. Dosage Related Reinforcement Responding for Females and Males Under Cocaine (0.0, 1.0, 2.0) and d-Amphetamine (0.0, 0.2, 0.4).

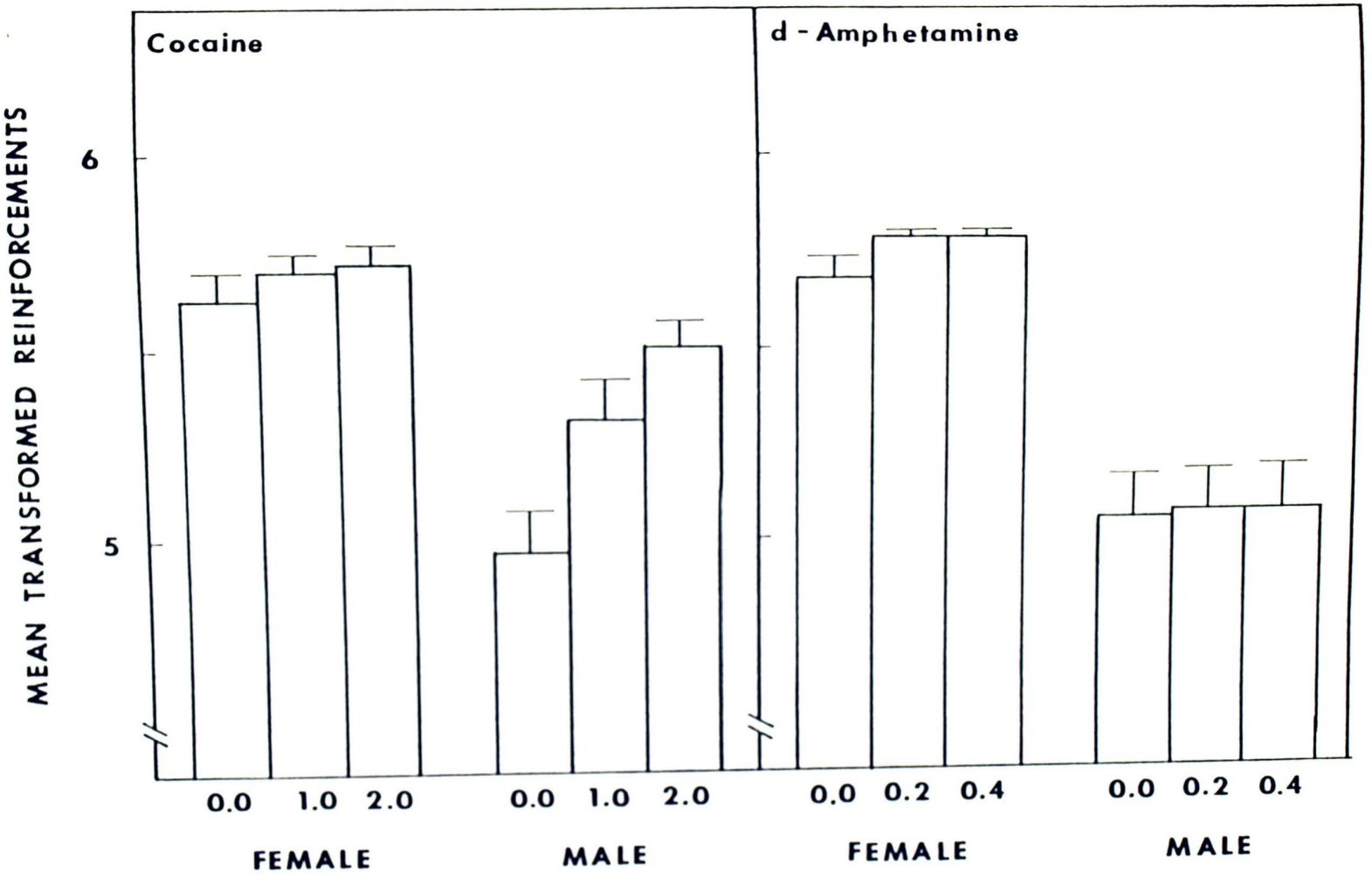
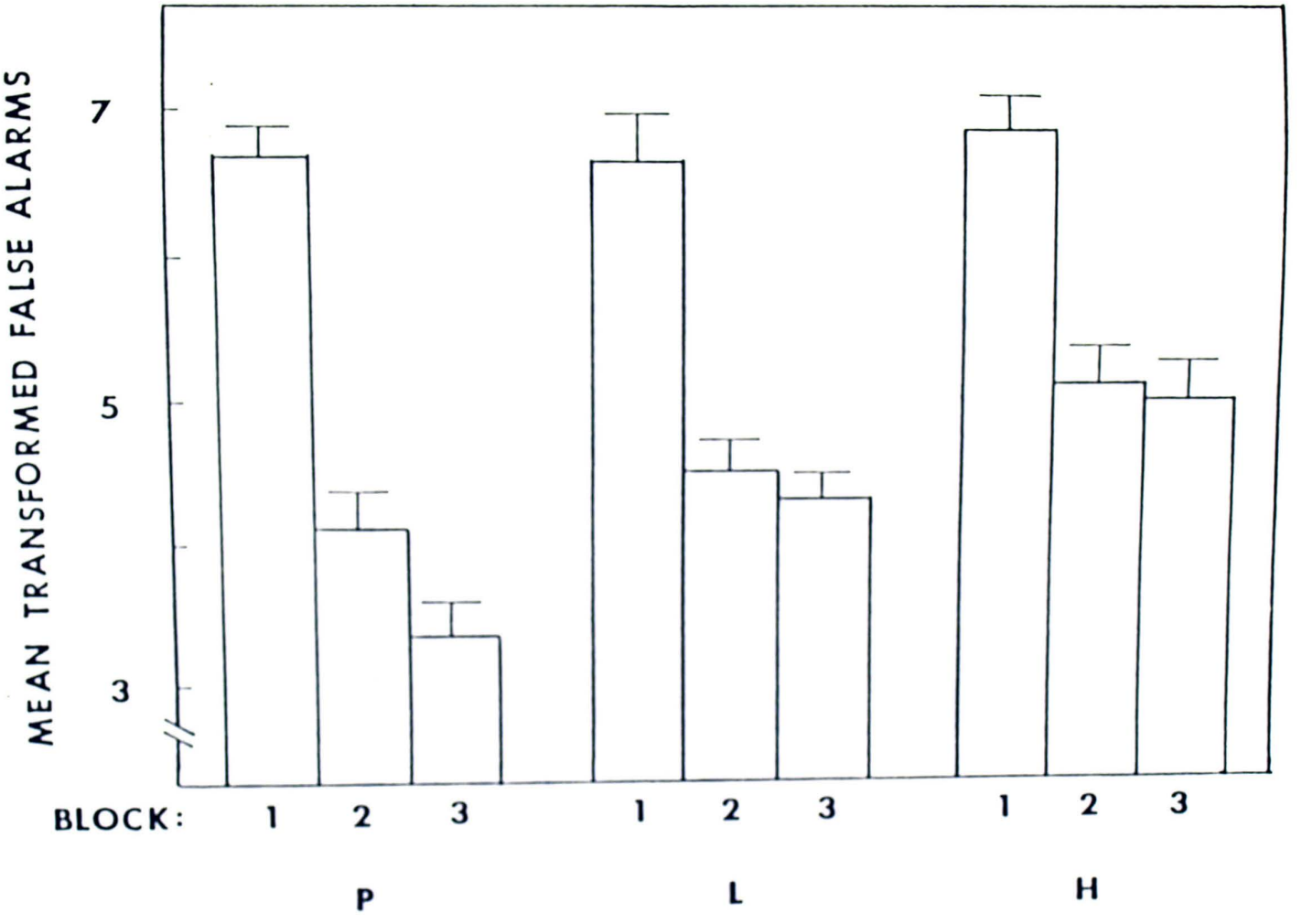

Cocaine
d - Amphetamine
MEAN TRANSFORMED REINFORCEMENTS
6
5
0.0
1.0
2.0
0.0
1.0
2.0
0.0
0.2
0.4
0.0
0.2
0.4
FEMALE
MALE
FEMALE
MALE

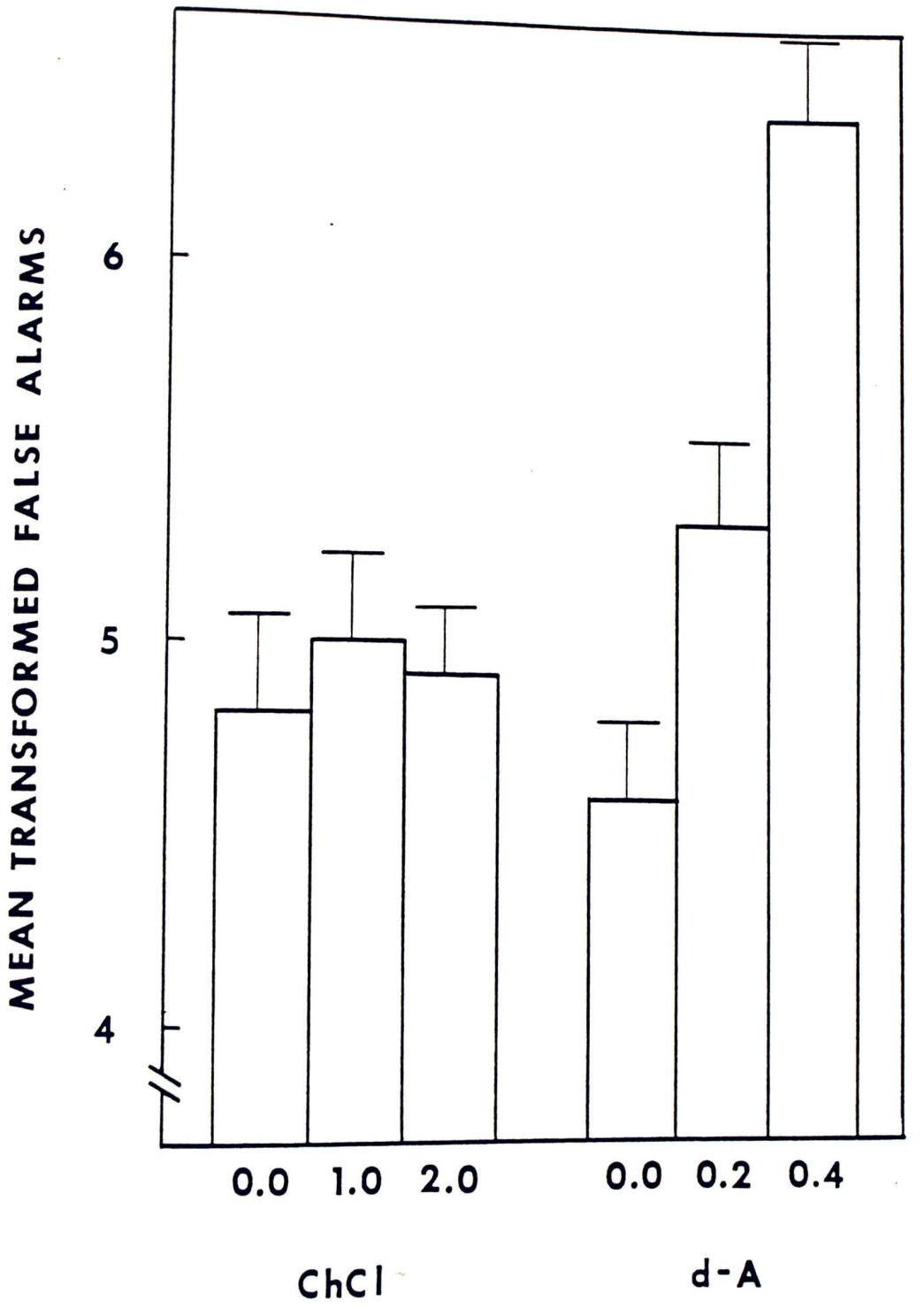
Figure 4. Combined Cocaine and d-Amphetamine Dosage Related (P=Placebo, L=Low, H=High) False Alarm Responding Across the Three 8 Trial Blocks.


MEAN TRANSFORMED FALSE ALARMS
7
5
3
BLOCK:
1
2
3
1
2
3
1
2
3
P
L
H

A significant interaction was obtained between drug type and dosage for false alarm responding, $F(2, 1060) = 13.62$, $p<.001$. No difference was found between cocaine and d-amphetamine on false alarm responding following the placebo or low dosage levels. It was found that d-amphetamine produced more false alarms at the high dosage than did cocaine, which produced no significant difference in false alarm response throughout all dosage levels, SRT, $\alpha=.01$ (see Figure 5).

Because a 10 second time-out period was employed in this design, a third analysis was done to see if this had any effect on the false alarm responding. A significant effect was found due to drug dosage, $F(2, 40) = 9.724$, $p<.001$, where increasing dosages extended the average false alarm time per trial. This effect was not independent of drug type, $F(2, 40) = 9.592$, $p<.001$. Cocaine produced no significant difference in the false alarm times, while d-amphetamine activated the 10 second time-out period more often with increasing dosage which resulted in a longer false alarm time per trial. These results support those found in the analysis of false alarms for the two drugs.

Figure 5. Dosage Related False Alarm Responding Under Cocaine (ChCl in mg/kg) and d-Amphetamine (d-A in mg/kg).


MEAN TRANSFORMED FALSE ALARMS
6
5
4
0.0
1.0
2.0
0.0
0.2
0.4
ChCl
d-A

CHAPTER 4

Discussion

Since cocaine and d-amphetamine are both classified as stimulants, most of the literature points out similarities between the two drugs. It has been demonstrated that both drugs increase arousal as measured by either EEG (Bradley, 1958) or increased locomotor activity (Kallman & Isaac, 1975; Seegal & Isaac, 1971; Wood & Golden, 1987). Also, cocaine and d-amphetamine both seem to produce their effects by using similar neurotransmitters (Scheel-Kruger, 1972). Along with these similarities, more recent evidence indicates some differences in the properties of these two drugs. Although both drugs increase locomotor activity, the activity tends to differ depending on both the drug employed and the familiarity of the testing environment (Miller et al., 1970; Scheel-Kruger et al., 1977). Discrepancies have also been reported in the neurochemical basis of action of the two drugs (Goldberg et al., 1970; Scheel-Kruger, 1972; Scheel-Kruger et al., 1977; Van Rossum, 1970; Van Rossum et al., 1962). The current evidence suggests that they act upon different aspects of the same neurotransmitters. It would appear that, in order to investigate the differing properties of cocaine and

d-amphetamine, in-depth research using relatively sensitive behavioral measures should be used.

The present study compared the effects of cocaine and d-amphetamine on vigilance performance. This attention based task is a more sensitive measure of arousal than gross locomotor activity. Even though both drugs are classified as stimulants, and produce grossly similar effects, a number of differences between them were found using the vigilance measure. Cocaine produced an increase in detection rate, while d-amphetamine did not. An earlier study, which reported d-amphetamine to increase the detection rate of rats (Squire & Golden, 1988), did not employ a 10 second non-response time-out. Because of this, Squire and Golden were unable to differentiate between increased overall responding and increased detection rate. In the present study, the 10 second time-out prevented a reinforcement from being earned due solely to an increase in overall responding. As a result, the increase in responding produced by d-amphetamine can be seen as an increase only in false alarms as compared to the stable false alarm rate produced by cocaine. This shows that d-amphetamine increases overall responding without increasing detection rate, while cocaine increases the detection rate without increasing overall responding.

The reason for including a 10 second pre-tone time-out in this design was to differentiate reinforcements earned due to attention from those reinforcements earned due to an increase in overall responding. Rats on d-amphetamine were found to extend the false alarm time by activating the 10 second pre-tone time-out more so than the rats on cocaine. This corresponds to the increase in false alarms seen with rats on d-amphetamine, but not in the cocaine animals. In addition to this, the cocaine animals received more reinforcements than the d-amphetamine animals demonstrating that cocaine increased the detection rate while d-amphetamine just increased overall arousal.

Furthermore, analysis of the detection rates indicated that males and females did not respond equally. The increase in detection rate produced by cocaine was seen mainly in the male rats, not the females. Although it has been reported that there are gender related differences in dopamine sensitivity (Gordon et al., 1980; Hruska et al., 1980) and the recovery rate of norepinephrine (Gordon & Shellenberger, 1974), little is known about the basis for these differences. The present study indicates the need to use subjects of both genders when conducting behavioral research with psychoactive substances.

Lynch and Carey (1986) recommend that within-sessions measures be used to examine the time course of drug effects

on behavior. In the present study trials within sessions were analyzed as three blocks of 8 trials each. It was found that the effects of the two drugs occurred primarily during the early portion of the session, decreasing rapidly from the first to the last block. This suggests that the effects of cocaine and d-amphetamine on vigilance performance, are relatively short lived. In addition, the two genders displayed different overall patterns of reinforcement responses within sessions. The males' detection rate decreased from the first to the third block, while the females detection rate remained constant throughout. Both of these findings support Lynch et al.'s suggestion concerning the need for within-sessions data. Furthermore, they indicate that behavioral studies using comparatively low dosages of centrally acting drugs and behavioral measures such as vigilance performance should take into account effects of both long and short duration.

Overall, the present study indicates that d-amphetamine and cocaine are indeed different in their effects on vigilance performance. Since both cocaine and d-amphetamine are classified as stimulants it would be assumed that these two drugs would cause similar effects. This is not the case according to this study. It appears that cocaine and d-amphetamine produce different types of reactions using a more sensitive measure such as vigilance.

It could also be assumed that both drugs operate on similar mechanisms in the brain. Although this may be true, this study shows that these mechanisms may be altered by the two drugs in different manners. Further research is needed in this area to explain the differences found by the present study.

APPENDIX

TABLE 1

Analysis of Variance for Reinforcements

SOURCE	SS	df	MS	F
TOTAL	1571.03	1295		
Between Groups	1076.99	23	46.82	
DRUG (A)	1.22	1	1.22	0.02
GENDER (B)	102.63	1	102.63	2.12
A x B	7.96	1	7.96	0.16
Error	965.17	20	48.25	
Within Treatments	494.03	1272	0.38	
TRIAL BLOCK (C)	2.03	2	1.01	2.68
A x C	5.70	2	2.85	7.54 ***
B x C	11.37	2	5.68	15.02 ***
A x B x C	1.48	2	0.74	1.96
REPLICATIONS (D)	2.45	5	0.49	1.29
A x D	2.06	5	0.41	1.09
B x D	2.92	5	0.58	1.54
A x B x D	1.19	5	0.23	0.63
DOSAGE (E)	7.87	2	3.93	10.40 ***
A x E	4.93	2	2.46	6.52 **
B x E	3.16	2	1.58	4.18 *
A x B x E	3.00	2	1.50	3.96 *
C x D	2.75	10	0.27	0.72
A x C x D	0.00	10	0.00	0.00
B x C x D	0.17	10	0.01	0.04
A x B x C x D	3.36	10	0.33	0.88
C x E	3.03	4	0.75	2.00
A x C x E	1.38	4	0.34	0.91
B x C x E	2.76	4	0.69	1.82
A x B x C x E	2.90	4	0.72	1.92
D x E	4.37	10	0.43	1.15
A x D x E	2.28	10	0.22	0.60
B x D x E	2.40	10	0.24	0.63
A x B x D x E	5.45	10	0.54	1.44

TABLE 1 (Continued)

SOURCE	SS	df	MS	F
C x D x E	3.22	20	0.16	0.42
A x C x D x E	4.61	20	0.23	0.61
B x C x D x E	4.47	20	0.22	0.59
A x B x C x D x E	1.47	20	0.07	0.19
error	401.11	1060	0.37	

* $p<.05$
** $p<.005$
*** $p<.001$

TABLE 2

Analysis of Variance for False Alarms

SOURCE	SS	df	MS	F
TOTAL	12023.58	1295		
Between Groups	1337.27	23	58.14	
DRUG (A)	86.28	1	86.28	1.49
GENDER (B)	84.32	1	84.32	1.46
A x B	11.93	1	11.93	0.20
Error	1154.73	20	57.73	
Within Treatments	10686.30	1272	8.40	
TRIAL BLOCK (C)	1637.32	2	818.66	124.72 ***
A x C	6.45	2	3.22	0.49
B x C	20.12	2	10.06	1.53
A x B x C	31.03	2	15.51	2.36
REPLICATIONS (D)	169.29	5	33.85	5.15 ***
A x D	56.10	5	11.22	1.70
B x D	111.35	5	22.27	3.39 *
A x B x D	85.21	5	17.04	2.59 *
DOSAGE (E)	189.35	2	94.67	14.42 ***
A x E	178.80	2	89.40	13.62 ***
B x E	39.22	2	19.61	2.98
A x B x E	28.72	2	14.36	2.18
C x D	86.33	10	8.63	1.31
A x C x D	37.90	10	3.79	0.57
B x C x D	32.97	10	3.29	0.50
A x B x C x D	51.69	10	5.16	0.78
C x E	75.64	4	18.91	2.88 *
A x C x E	32.23	4	8.05	1.22
B x C x E	26.26	4	6.56	1.00
A x B x C x E	51.60	4	12.90	1.96
D x E	129.56	10	12.95	1.97
A x D x E	66.72	10	6.67	1.01
B x D x E	67.69	10	6.76	1.03
A x B x D x E	88.68	10	8.86	1.35

TABLE 2 (Continued)

SOURCE	SS	df	MS	F
C x D x E	63.87	20	3.19	0.48
A x C x D x E	104.12	20	5.20	0.79
B x C x D x E	149.83	20	7.49	1.14
A x B x C x D x E	110.29	20	5.51	0.84
error	6957.82	1060	6.56	

* $p<.05$
** $p<.005$
*** $p<.001$

TABLE 3

Analysis of Variance for Extended False Alarm Times

SOURCE	SS	df	MS	F
TOTAL	66728.21	1295		
Between Groups	6880.51	23	299.15	
DRUG (A)	1056.24	1	1056.24	3.66
GENDER (B)	60.49	1	60.49	0.21
A x B	1.00	1	1.00	0.00
Error	5762.77	20	288.13	
Within Treatments	59847.70	1272	47.05	
TRIAL BLOCK (C)	2166.99	2	1083.49	18.34 **
A x C	195.68	2	97.84	1.65
B x C	160.42	2	80.21	1.35
A x B x C	494.09	2	247.04	4.18 *
REPLICATIONS (D)	775.20	5	155.04	2.97 *
A x D	485.10	5	97.02	1.86
B x D	316.08	5	63.21	1.21
A x B x D	217.42	5	43.48	0.83
DOSAGE (E)	1584.19	2	792.09	9.72 **
A x E	1562.79	2	781.39	9.59 **
B x E	157.89	2	78.94	0.96
A x B x E	51.49	2	25.74	0.31
C x D	397.38	10	39.73	1.13
A x C x D	87.93	10	8.79	0.25
B x C x D	275.19	10	27.51	0.78
A x B x C x D	325.94	10	32.59	0.92
C x E	88.71	4	22.17	0.53
A x C x E	270.59	4	67.64	1.62
B x C x E	44.91	4	11.29	0.27
A x B x C x E	185.55	4	46.38	1.11
D x E	509.10	10	50.91	1.02
A x D x E	406.35	10	46.63	0.93
B x D x E	605.03	10	60.50	1.21
A x B x D x E	528.35	10	52.83	1.06

TABLE 3 (Continued)

SOURCE	SS	df	MS	F
C x D x E	389.37	20	19.46	0.55
A x C x D x E	496.20	20	24.81	0.70
B x C x D x E	900.04	20	45.00	1.28
A x B x C x D x E	937.70	20	46.88	1.33
error	45171.89	1060	42.61	

* $p<.05$
** $p<.001$

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