EFFECTS OF COCAINE ON THE ABILITY OF RATS TO HABITUATE TO A NOVEL ENVIRONMENT

MARCIA CAROLE WOOD

EFFECTS OF COCAINE ON THE ABILITY OF RATS TO HABITUATE TO A NOVEL ENVIRONMENT

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

---

by

Marcia Carole Wood

December 1986

ABSTRACT

The behavioral effects of cocaine use in humans include psychomotor agitation, elation, and hypervigilance (American Psychiatric Association [APA], 1980). Physical symptoms representing activation of the sympathetic division of the central nervous system are also typical of cocaine use (APA). In rats, cocaine is typically reported to be a locomotor stimulant. Scheel-Kruger et al. (1977) reported that the increase in activity following cocaine administration in rats was weak and unpredictable when the animals were kept in a familiar environment. When the animals were placed in a novel environment following cocaine administration however, they showed high and sustained locomotor activity suggesting that cocaine might interfere with the ability to habituate to novel environmental stimuli.

Ambient sensory stimuli alone, such as illumination and noise, have been reported to produce behavioral arousal in the form of increased locomotor activity (Delay, 1985; Isaac & Devito, 1958). In addition, the illumination level present during testing has been demonstrated to interact with the effects of several stimulant drugs other than cocaine (Isaac & Troelstrup, 1969; Kallman & Isaac, 1975). However, the effects of sensory stimuli are not stable over repeated presentations (Kallman & Isaac, 1977). These

researchers suggested that this change was a result of habituation across sessions. Delay (1981) found that activity levels declined progressively within sessions and suggested that this effect may also have been a result of habituation.

The present study, in a series of two experiments, measured the effects of cocaine on the locomotor activity of rats exposed to both the light and the dark and in the presence of pulsed white masking noise as a novel sensory stimulus. Habituation to this novel stimulus was examined using the method developed by Wood (1984).

In Experiment 1, ten male and ten female CD rats received intraperitoneal injections of four different dosages (0.0, 7.5, 15.0, 30.0 mg/kg) of cocaine HCl every third test day in a pseudo-random order. On the intervening non-drug days all rats were given intraperitoneal injections of the isotonic saline vehicle and tested. Illumination conditions of light and dark were alternated every third day. Locomotor activity increased significantly from 0.0 mg/kg to the 7.5 mg/kg dosage and from the 7.5 mg/kg to the 15 mg/kg dosage. Activity in the dark condition was significantly greater than activity in the light condition at the 0.0 mg/kg and the 7.5 mg/kg dosages. Activity levels at the two highest dosages, however, were greater in the light condition than in the dark condition. Cocaine dosage also interacted significantly with 10 minute intervals within sessions. The activity levels at the 0.0 mg/kg and

the 7.5 mg/kg dosages declined significantly across the intervals, primarily from the first to the third intervals. At the two highest cocaine dosages, the decline of activity levels across intervals was not present. Analysis of the data from the two intervening non-drug days revealed a significant main effect for cocaine dosage on the first day following drug administration and no such effect on the second non-drug day.

In the second experiment, 18 male and 18 female CD rats were exposed to 75db SPL of pulsed white masking noise in 5 minute intervals alternated with 5 minute intervals of quiet. The starting condition of quiet or noise was rotated for each test session. All of the rats were assigned to one of two groups, placebo (isotonic saline) or 15 mg/kg cocaine HCl in isotonic saline. Testing was conducted every other day to avoid any carryover effects of the drug. The rats in the cocaine group were more active than the rats in the placebo group. The activity levels of both groups were higher during those portions of the test sessions in which noise was present. Female rats in the cocaine group were more active than male rats in the cocaine group, while the two genders did not differ in the placebo group. The female rats receiving cocaine were more active when started in the noise than in the quiet, while the male rats receiving cocaine and all rats in the placebo group did not differ between the two starting conditions.

LIST OF TABLES

EFFECTS OF COCAINE ON THE ABILITY OF RATS TO HABITUATE TO A NOVEL ENVIRONMENT

A Thesis

Presented to the

Graduate and Research Council of

Austin Peay State University

In Partial Fulfillment

of the Requirements for the Degree

Master of Arts

---

by

Marcia Carole Wood

December 1986

To the Graduate and Research Council:

I am submitting herewith a Thesis written by Marcia Carole Wood entitled "Effects of Cocaine on the Ability of Rats to Habituate to a Novel Environment." 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

ACKNOWLEDGEMENTS

I wish to express my tremendous appreciation and gratitude to Dr. Anthony Golden for his guidance, support and his unlimited patience throughout the duration of this thesis.

I wish to thank my other committee members, Dr. Susan Kupisch and Dr. Garland Blair for their time and advice.

I wish also to thank Ms. Linda Freed for her advice, cooperation and understanding through the completion of this thesis.

TABLE OF CONTENTS

LIST OF FIGURES

FIGURE PAGE

CHAPTER 1

Review of the Literature

History and Behavioral Effects of Cocaine

The effects of cocaine on the central nervous system were first described by Aschenbrandt in 1883 and by Freud in 1884 (cited in Van Dyke & Byck, 1977). The anesthetic effects of cocaine were discovered by Koller in 1884 (cited in Van Dyke & Byck). However, the mechanism of action and its effects on the central nervous system are still not well documented (Van Dyke & Byck).

The behavioral effects of cocaine use in humans, according to the DSM III (American Psychiatric Association [APA], 1980), include psychomotor agitation, elation, grandiosity, loquacity, and hypervigilance. These effects are typically seen within one hour of use regardless of route of administration. The DSM III (APA) reports that the physical symptoms of cocaine use include tachycardia, pupillary dilation, elevated blood pressure, perspiration or chills, nausea and vomiting. All of these are symptoms of the activation of the sympathetic division of the autonomic nervous system. In addition, cocaine use can have an anorexigenic effect in humans and animals. Also according to the DSM III (APA), maladaptive behavioral effects in humans include "fighting, impaired judgement, and interference with social or occupational functioning" (APA,

p. 146). Severe cocaine intoxication can produce incoherent speech and anxiety and, in high dosages, cocaine has also been reported to produce paranoid ideations (APA). There is no known withdrawal syndrome associated with cocaine use.

Research on the development of tolerance to cocaine is contradictory (Epstein & Altshuler, 1978; Van Dyke & Byck, 1977). There is some evidence which suggests that a tolerance does develop to some of the convulsant effects that are associated with cocaine use (Epstein & Altshuler). There is also research which suggests that a sentization occurs to some of the behavioral of cocaine use (Epstein & Altshuler; Van Dyke & Byck). Epstein & Altshuler reported that there may be sensitization to the behavioral effects of cocaine and a tolerance that occurs to some of the other effects of cocaine such as the convulsant effects.

Research on the behavioral and effects of cocaine in animals is also contradictory. It is possible that the effects of cocaine differ depending on the species of animal, dose, route of administration, the schedule of drug administration and method of observation. Each of these factors varies greatly among the many experiments conducted using cocaine and animals (Van Dyke & Byck, 1977). Therefore, agreement exists only on some of the more general effects.

Cocaine appears to produce a short term increase in activity immediately following administration (Ho, Taylor, Estevez, Englert, & Mc Kenna, 1977; Scheel-Kruger,

Braestrup, Nielson, Golembiowska & Mogilnicka, 1977; Van Dyke & Byck, 1977; Wallach & Gershon, 1971). In high dosages, cocaine induces stereotypy (Macphail & Seiden, 1975; Van Dyke & Byck; Wallach & Gershon). It has been reported that rats and monkeys can be trained to self administer cocaine and that they will perform work in order to receive the drug (Macphail & Seiden; Van Dyke & Byck). Scheel-Kruger et al. reported that the increase in activity following cocaine administration in rats was weak and unpredictable when the animals were kept in a familiar environment. However, any sudden noise or tactile stimulation would produce an abrupt, short term increase in locomotor activity. When the animals were placed in a novel environment following cocaine administration, they showed high and sustained locomotor activity. It is possible, therefore, that cocaine interferes with the ability to habituate to novel sensory stimulation or to novel environments.

Ambient Sensory Stimulation

It has been reported that ambient sensory stimuli, such as illumination and noise, produce behavioral arousal in the form of increased locomotor activity (Isaac & Devito, 1958). Isaac and Devito reported that the activity levels of diurnal monkeys were influenced by both light and noise. These researchers found that noise increased activity levels, however, only in the presence of illumination.

Isaac and Reed (1961) examined the effects of noise on the activity levels of cats. They reported that noise increased activity levels in the light and that while activity levels were generally higher in the dark they were not significantly increased by the noise. Using human subjects, Kallman and Isaac (1977) tested reaction times in the presence of noise in both the light and the dark. They reported that noise served to increase reaction times in the light, but that no effect of noise was found in the dark. Delay (1985) also reported increased activity levels of rats in the presence of noise. However, Delay reported finding this effect in both the light and the dark in 25 day old animals.

Habituation to Sensory Stimulation

The effects of sensory stimuli, however, are not stable over repeated presentations. Kallman and Isaac (1977) reported that the reaction times of their human subjects decreased across replications which were three to eight weeks apart. These researchers suggested that this change was a result of habituation across sessions. Delay (1981) reported being able to obtain changes in locomotor activity levels with rats across 10 minute intervals within a 60 minute test session. He found that activity levels declined progressively across the intervals within sessions. Delay suggested that this effect may also have been a result of habituation.

Other Stimulant Drug Effects

The effects of stimulant drugs other than cocaine, such as d-amphetamine and methylphenidate have been demonstrated to interact with ambient illumination present during testing (Alexander & Isaac, 1965; Isaac & Troelstrup, 1969; Kallman & Isaac, 1975; Lowther & Isaac, 1976). However, no such interaction has yet been demonstrated using cocaine.

Purpose of the Present Study

The present study examined the effects of cocaine on the locomotor activity of rats in a series of two experiments. The first measured the effects of ambient illumination on the locomotor activity response to cocaine. The second examined the locomotor activity of rats receiving cocaine in the presence of pulsed white masking noise as a novel sensory stimulus. The rats' ability to habituate to this novel stimulus was measured using the method developed by Wood (1984).

CHAPTER 2

Experiment 1

Method

Subjects

Ten male and 10 female CD rats born of gravid females obtained from Charles River Laboratories served as subjects. All of the rats were approximately 129 days of age at the beginning of testing. The rats were housed individually under a LD 12:12 lighting schedule with food and water available ad lib.

Apparatus

The rats were tested in 20.5 x 22.5 x 44.0 cm clear plastic cages with 6 mm hardware cloth tops. All of the cages were placed into 56.0 x 51.0 x 70.0 cm individual sound attenuating cubicles which were open at the front. Illumination was provided by 20w fluorescent lamps mounted above the center of each cubicle. An infrared beam bisected the long axis of the cage 3 cm above its floor as suggested by Isaac and Ruch (1956) for accuracy in measuring activity data. Beam breaks were recorded in twelve 5 minute intervals by an Advanced Digital Super Six single board computer located in a separate room. Ambient noise measured 45 db SPL (A scale, re: 20 $\mu N/m^2$).

Procedure

Assignment of the rats to the test cubicles was sex balanced. Starting with the first day of testing and continuing every third day thereafter, each rat received an intraperitoneal injection (1 ml/kg body weight) of one of four dosages (0.0, 7.5, 15, 30 mg/kg) of cocaine HCl (Sigma Chemical Co.) in an isotonic saline vehicle. The four cocaine dosages were presented in a pseudo-random order such that none of the dosages followed the same dosage in order of presentation. Testing continued until all of the rats had received all four dosages under both illumination conditions. At this time, the conditions were replicated using a different order of drug presentations. Cocaine was administered a total of 16 times over a period of 48 days. On the intervening non-drug days, all rats received intraperitoneal injections (1 ml/kg) of isotonic saline and were tested in order to measure any carryover effects of the cocaine. All of the injections were administered immediately prior to the test sessions. Ambient illumination conditions of light (1,076 lx) and dark (<10.76 lx) were alternated on each drug day (every three test days) so that each continued through the two succeeding non-drug days.

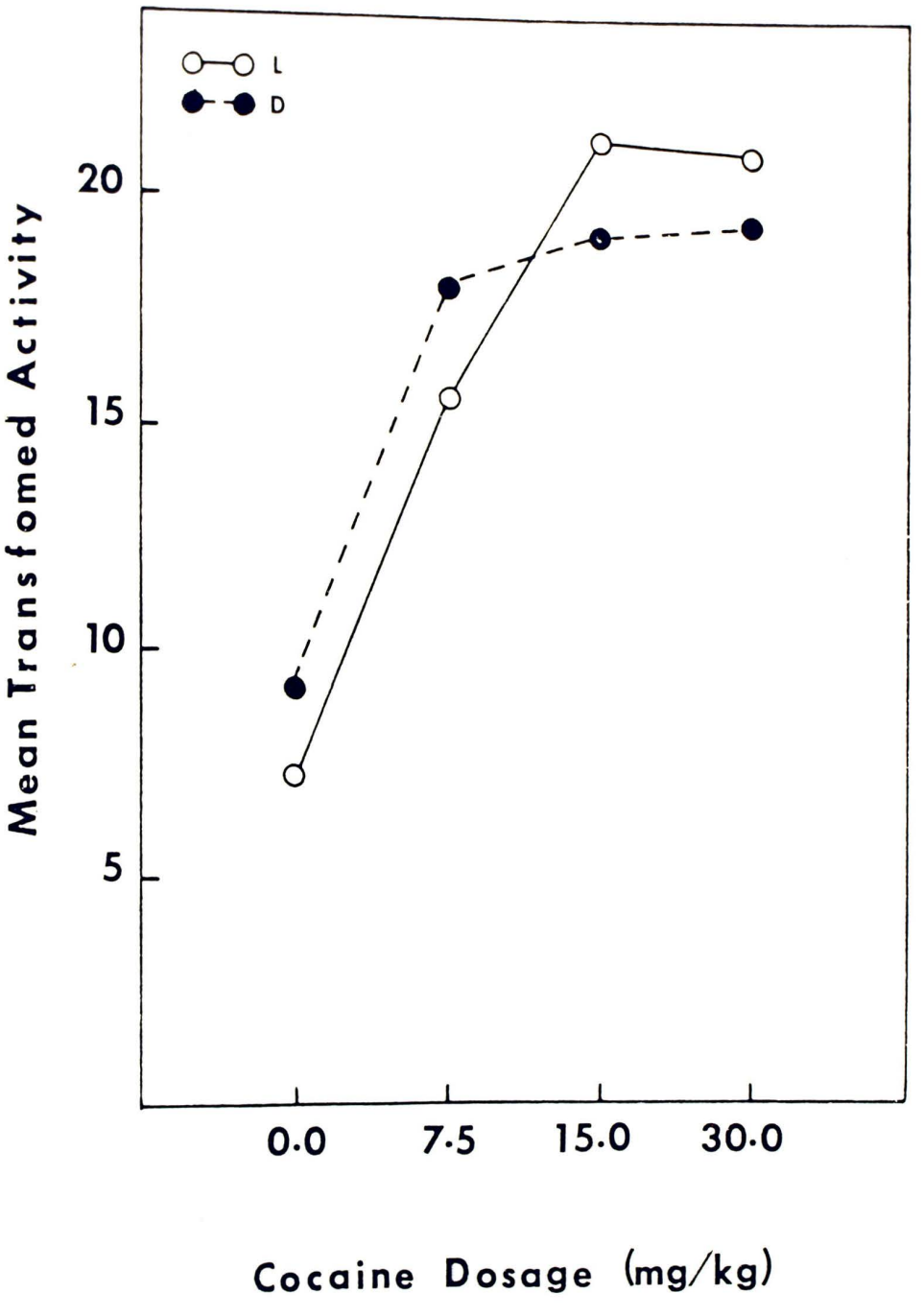
CHAPTER 3

Results of Experiment 1

The data were transformed to the $\sqrt{X} + \sqrt{X + 1}$ as recommended by Edwards (1985) for frequency data and subjected to an analysis of variance (see Table 1). Further analyses were conducted using either simple effects analysis of variance or Duncan's Multiple Range Test (DMR).

The analysis revealed a significant main effect for cocaine dosage, $F(3, 1710) = 350.2$, $p<.001$, such that activity increased from 0.0 mg/kg (placebo) to the 7.5 mg/kg dosage and from the 7.5 mg/kg to the 15 mg/kg dosage, DMR, $\alpha = .01$. No further increase was observed at the 30 mg/kg dosage. An interaction of cocaine dosage with illumination was also obtained, $F(3, 1710) = 15.1$, $p<.01$, (see Figure 1). Simple effects analysis revealed that activity in the dark condition was significantly greater than activity in the light condition at the 0.0 mg/kg, $F(1, 1710) = 10.0$, $p<.005$, and the 7.5 mg/kg dosages, $F(1, 1710) = 17.1$, $p<.005$. Activity levels at the 15 mg/kg, $F(1, 1710) = 11.7$, $p<.005$, and 30 mg/kg dosages, $F(1, 1710) = 6.8$, $p<.01$, however, were greater in the light condition than in the dark condition. A significant main effect was obtained for replications such that overall levels of activity were higher in the first replication than in the second replication, $F(1, 1710) = 83.4$, $p<.01$. An interaction was also obtained between

Figure 1. Effects of cocaine on locomotor activity under illumination conditions of light and dark.

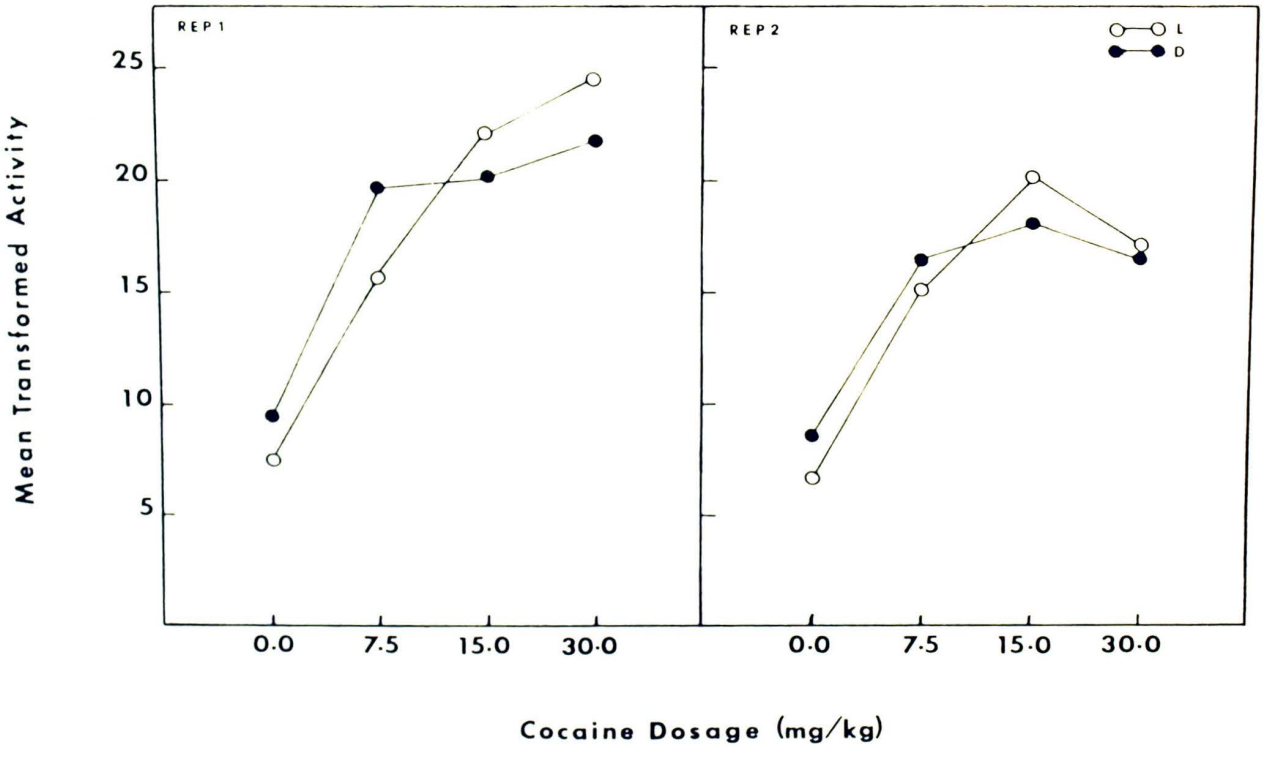

L
D
20
15
10
5
Mean Transfomed Activity
0.0
7.5
15.0
30.0
Cocaine Dosage (mg/kg)

cocaine dosage and replications, $F(3, 1710) = 16.2$, $p<.01$. Simple effects analysis revealed that levels of activity under the highest cocaine dosage (30 mg/kg) decreased from the first to the second replication, $F(1, 1710) = 110.3$, $p<.001$. Activity levels at the three other dosages, however, did not differ between the two replications, $p>.05$.

An interaction of cocaine dosage with illumination and replications was obtained, $F(3, 1710) = 2.7$, $p<.05$. Simple effects analysis revealed that illumination interacted with replications at the 7.5 mg/kg, $F(1, 1710) = 3.9$, $p<.05$, and the 30 mg/kg dosages only, $F(1, 1710) = 4.0$, $p<.05$. In the first replication the levels of activity were significantly higher in the dark than in the light under the 7.5 mg/kg drug dosage, $F(1, 1710) = 18.7$, $p<.01$. The levels of activity in the second replication did not differ between the two illumination conditions at the 7.5 mg/kg dosage, $p>.05$, (see Figure 2). At the 30 mg/kg cocaine dosage, activity levels were higher in the light than in the dark in the first replication, $F(1, 1710) = 10.7$, $p<.01$. In the second replication, however, no difference in activity levels between the two illumination conditions was found for this dosage, $p>.05$. No significant interaction was obtained between illumination and replications for the 0.0 mg/kg, or the 15 mg/kg dosages, $F<1$.

A significant main effect was obtained for the 10 minute intervals within sessions, $F(5, 1710) = 151.8$, $p<.01$. Locomotor activity declined within sessions primarily across

Figure 2. Changes in the locomotor response to cocaine under illumination conditions of light and dark for the two replications.


REP 1
REP 2
L
D
25
20
15
10
5
0·0
7·5
15·0
30·0
0·0
7·5
15·0
30·0
Mean Transformed Activity
Cocaine Dosage (mg/kg)

the first 3 of the 6 intervals. Activity declined significantly from the first to the second interval and from the second to the third interval, DMR, $\alpha = .01$. Activity levels did not differ across the last three 10 minute intervals within the 60 minute test session. Cocaine dosage also interacted significantly with intervals, $F(15, 1710) = 6.8$, $p<.01$, (see Figure 3). The level of activity under the 0.0 mg/kg dosage declined rapidly across the first 3 of the 6 intervals. The 7.5 mg/kg cocaine dosage produced a similar decline across the intervals although the levels of activity remained somewhat higher than those at the 0.0 mg/kg dosage. At the two highest cocaine dosages, however, the decline of activity levels across intervals was not present. This was the case particularly at the highest dosage (30 mg/kg) where activity levels dropped slightly after the first interval but remained fairly constant across the remaining 5 intervals.

Analysis of the data from the two intervening non-drug days (see Tables 2 and 3) revealed a significant effect for cocaine dosage on the first day following drug administration, $F(3, 1710) = 9.8$, $p<.001$, (see Figure 4). No such effect, however, was evident in the data from the second non-drug day, $p>.05$. Illumination main effects were obtained for both the first, $F(1, 1710) = 116.7$, $p<.001$, and second days, $F(1, 1710) = 117.2$, $p<.001$, between cocaine administrations (see Figure 5). On both non-drug days,

Figure 3. Locomotor activity levels under the four cocaine dosage levels across the six 10 minute intervals within sessions.

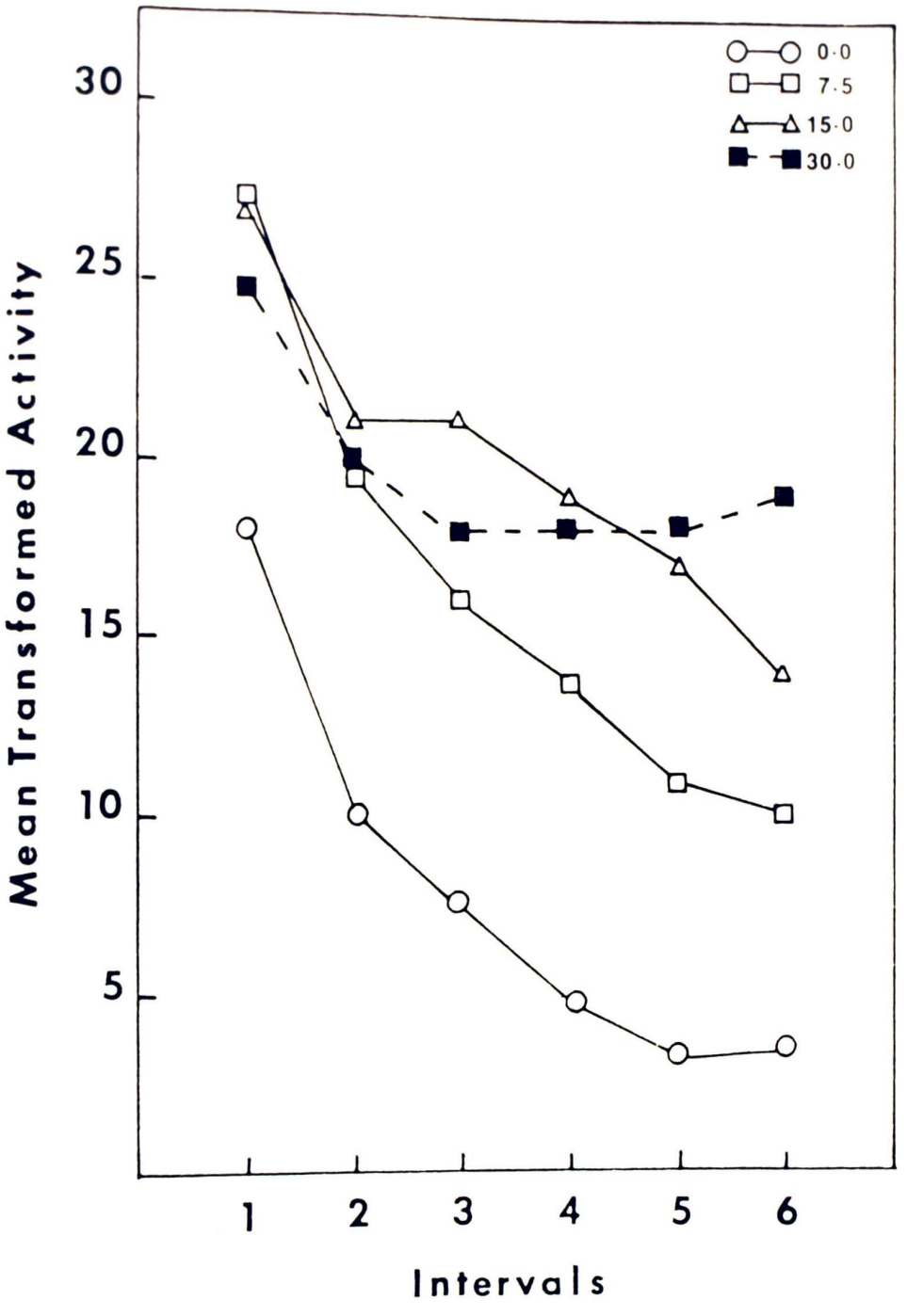

0·0
7·5
15·0
30·0
30
25
20
15
10
5
Mean Transformed Activity
1
2
3
4
5
6
Intervals

Figure 4. Cocaine dose effects obtained on non-drug day 1 (ND1) and non-drug day 2 (ND2).

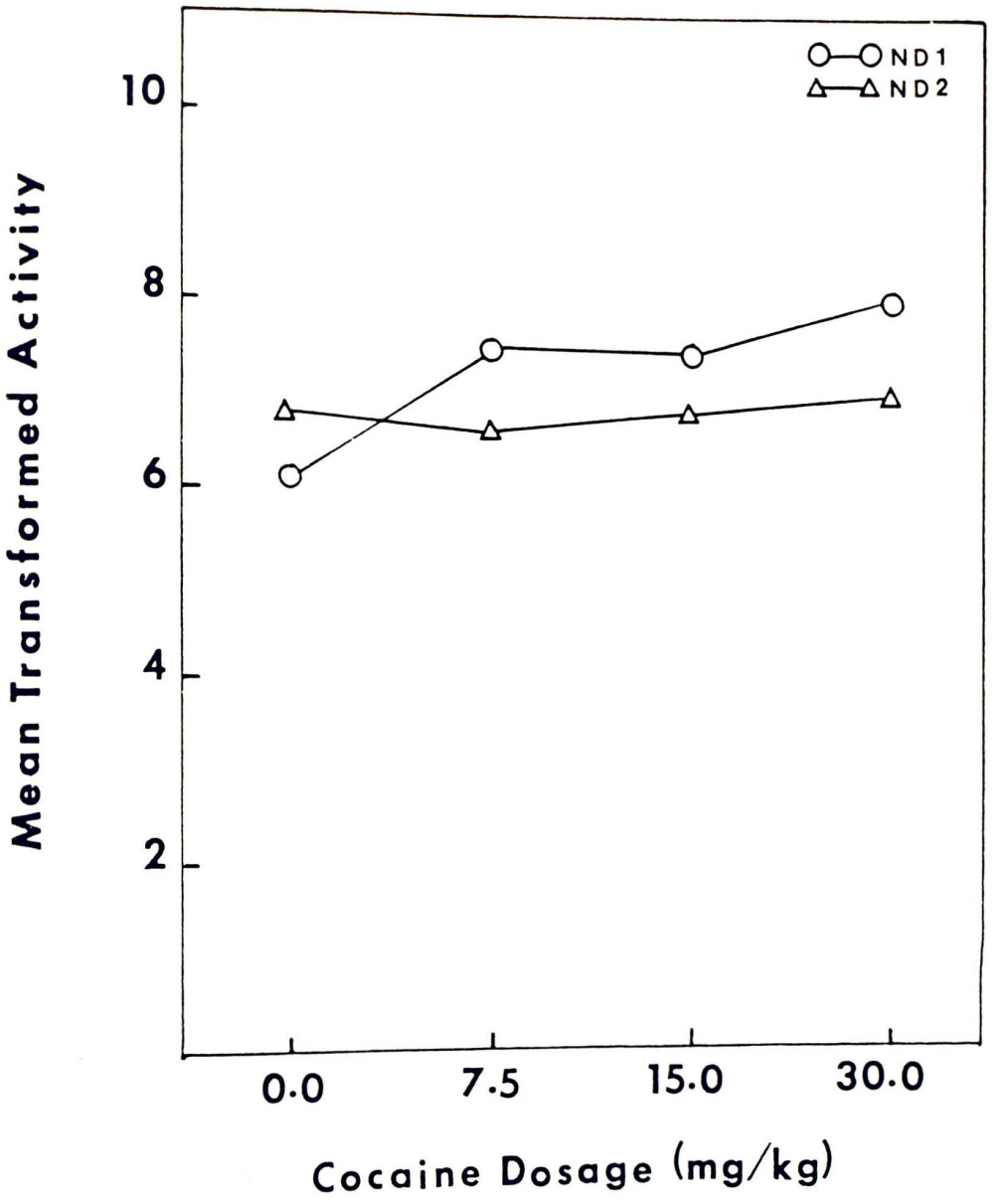
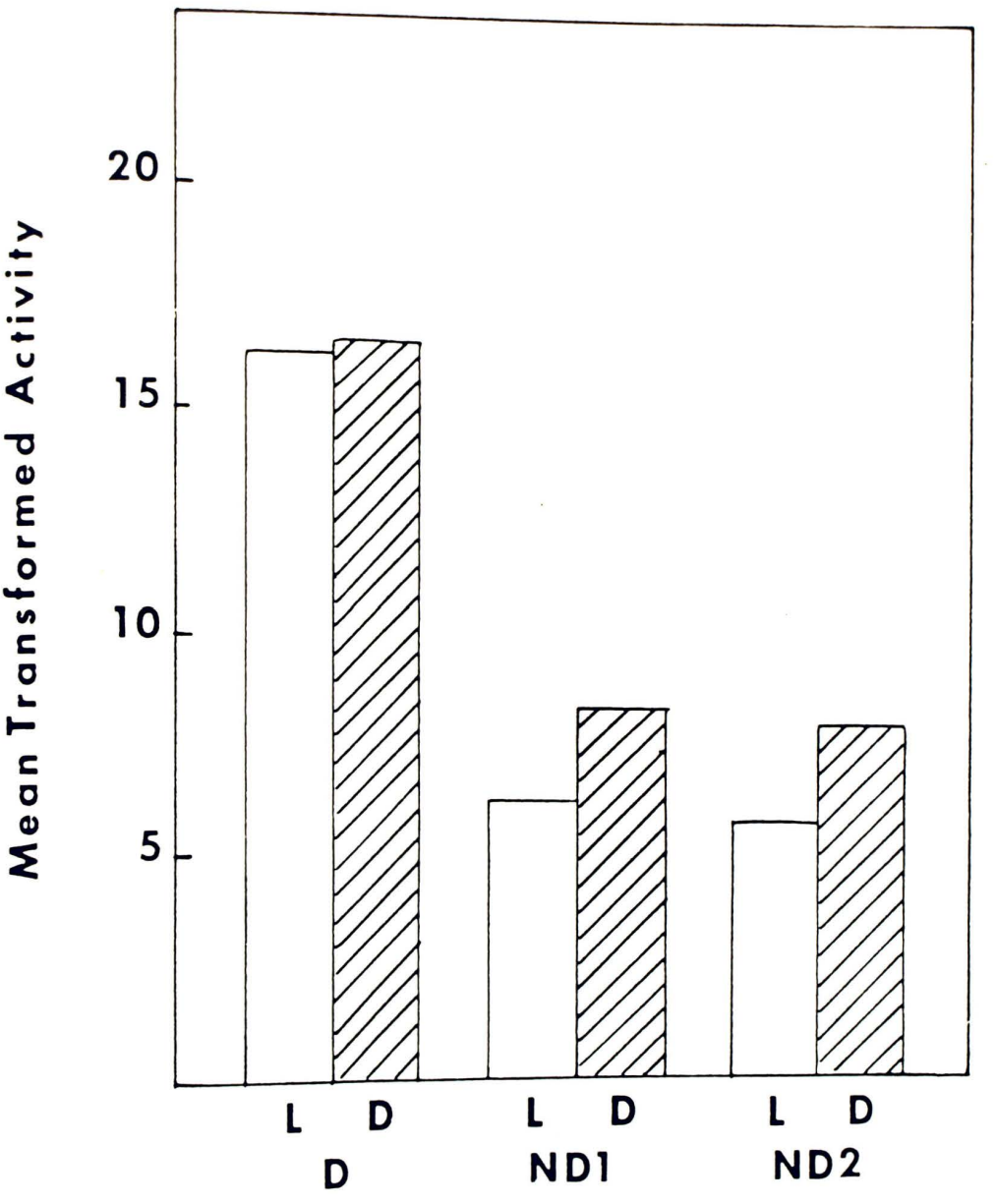

ND1
ND2
Mean Transformed Activity
10
8
6
4
2
0.0
7.5
15.0
30.0
Cocaine Dosage (mg/kg)

Figure 5. Locomotor activity levels in the light and dark obtained on drug days (D) and on the first (ND1) and second (ND2) non-drug days.


Mean Transformed Activity
20
15
10
5
L
D
L
D
L
D
D
ND1
ND2

activity levels were significantly higher in the dark than in the light condition.

CHAPTER 4

Experiment 2

Method

Subjects

Eighteen male and 18 female CD derived rats, born and bred at Austin Peay State University, served as subjects. All of the rats were weaned at 21 days of age and were approximately 140 days of age at the beginning of testing. All of the rats were housed individually under a LD 12:12 lighting schedule with food and water available ad lib.

Apparatus

The rats were tested in 20.5 x 22.5 x 44.0 cm clear plastic cages with 6 mm hardware cloth tops. All cages were placed into 56.0 x 51.0 x 70.0 cm individual sound attenuating cubicles which were open at the front. Illumination (1,076 lx) was provided by 20w fluorescent lamps mounted above the center of each cubicle. An infrared beam bisected the long axis of the cage 3 cm above its floor as suggested by Isaac and Ruch (1956) for accuracy in measuring activity data. Beam breaks were recorded in twelve 5 minute intervals by an Advanced Digital Super Six single board computer located in a separate room. Ambient noise during the quiet condition measured 45 db SPL (A scale, re: 20 $\mu N/m^2$). The masking noise, 75 db SPL (A scale,

re: 20 $\mu N/m^2$), was produced by a Texas Instruments 76477 integrated circuit through a Newcomb Type 1020 vacuum tube amplifier. Solid state programming equipment was used to control the onset and offset of the noise, 1 second on/ 1 second off (50% duty cycle).

Procedure

Assignment of the rats to the test cubicles was sex balanced. All of the rats were exposed to the pulsed white masking noise in 5 minute intervals alternated with 5 minute intervals of quiet. The starting condition of quiet or noise was rotated for each test session with the first session starting in the quiet.

All of the rats were assigned to one of two groups, placebo (isotonic saline) or cocaine (15 mg/kg cocaine HCl in isotonic saline). The two groups received intraperitoneal injections (1 ml/kg body weight) immediately prior to each test session. Based upon the findings of Experiment 1, testing was conducted every other day to avoid any carryover effects of the drug. Testing continued for a total of 16 sessions.

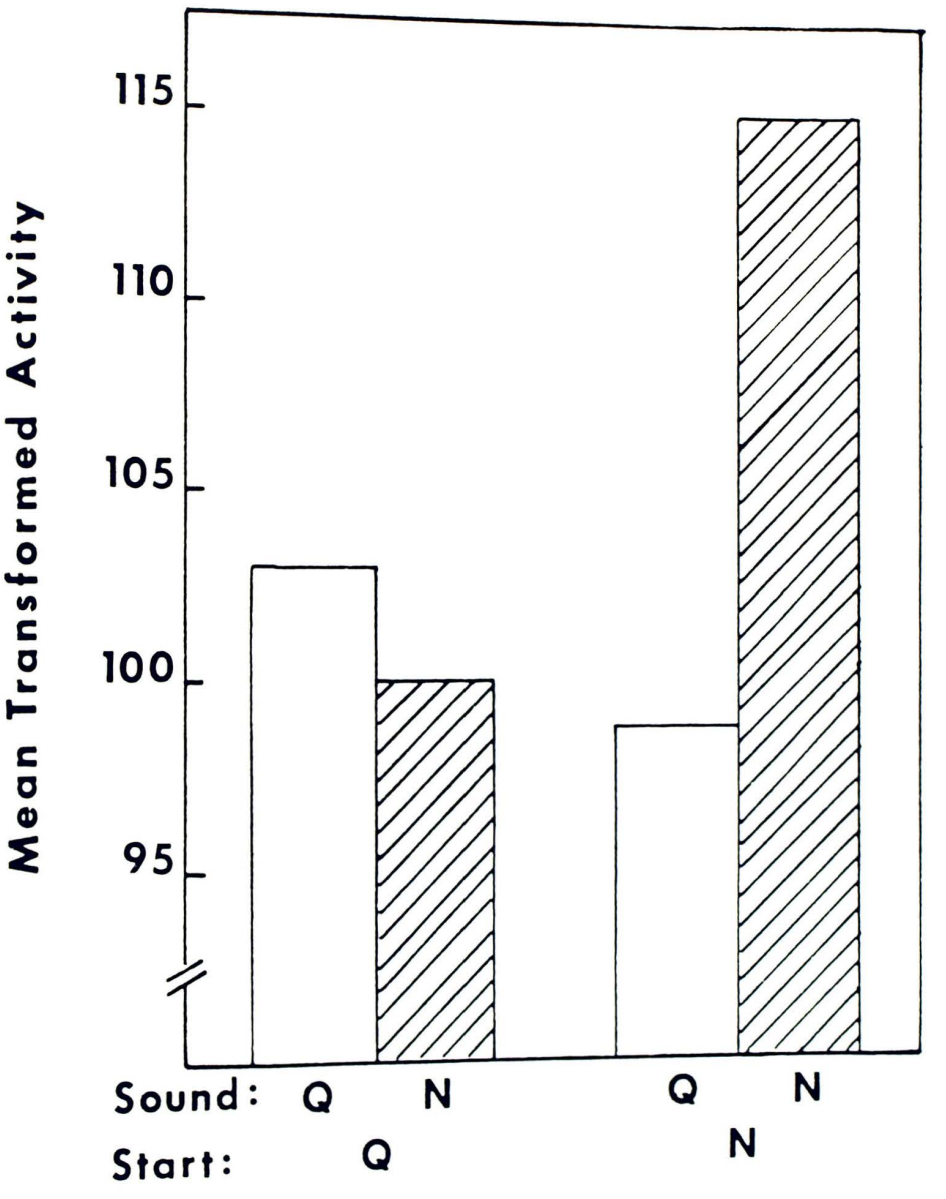
CHAPTER 5

Results of Experiment 2

The data were transformed to the $\sqrt{X} + \sqrt{X + 1}$ as recommended by Edwards (1985) for frequency data. The data were collapsed across intervals and across days into four 4 day blocks. The data were then subjected to an analysis of variance (see Table 4). Further analyses were conducted using either simple effects analysis of variance or Duncan's Multiple Range Test (DMR).

The data indicated that the rats were significantly more active during those portions of the test sessions in which noise was present, $F(1, 32) = 8.4$, $p<.005$. Also, the rats exhibited significantly higher overall levels of activity during sessions which began with the pulsed noise on, $F(1, 32) = 9.4$, $p<.005$. The effects of these two variables, however, were not independent of each other, $F(1, 32) = 97.0$, $p<.001$. Further analysis revealed that activity levels across noise conditions did not differ when sessions begin with the pulsed noise off. However, when sessions began with the pulsed noise on, activity levels in the noise portions of the test session were significantly higher than under any other condition, DMR, $\alpha = .01$, (see Figure 6.). A significant main effect was obtained for day blocks, $F(3, 96) = 24.5$, $p<.001$, such that activity increased significantly from the first block of 4 days to

Figure 6. Activity levels under quiet and noise sound conditions within sessions starting either in the quiet or the noise.

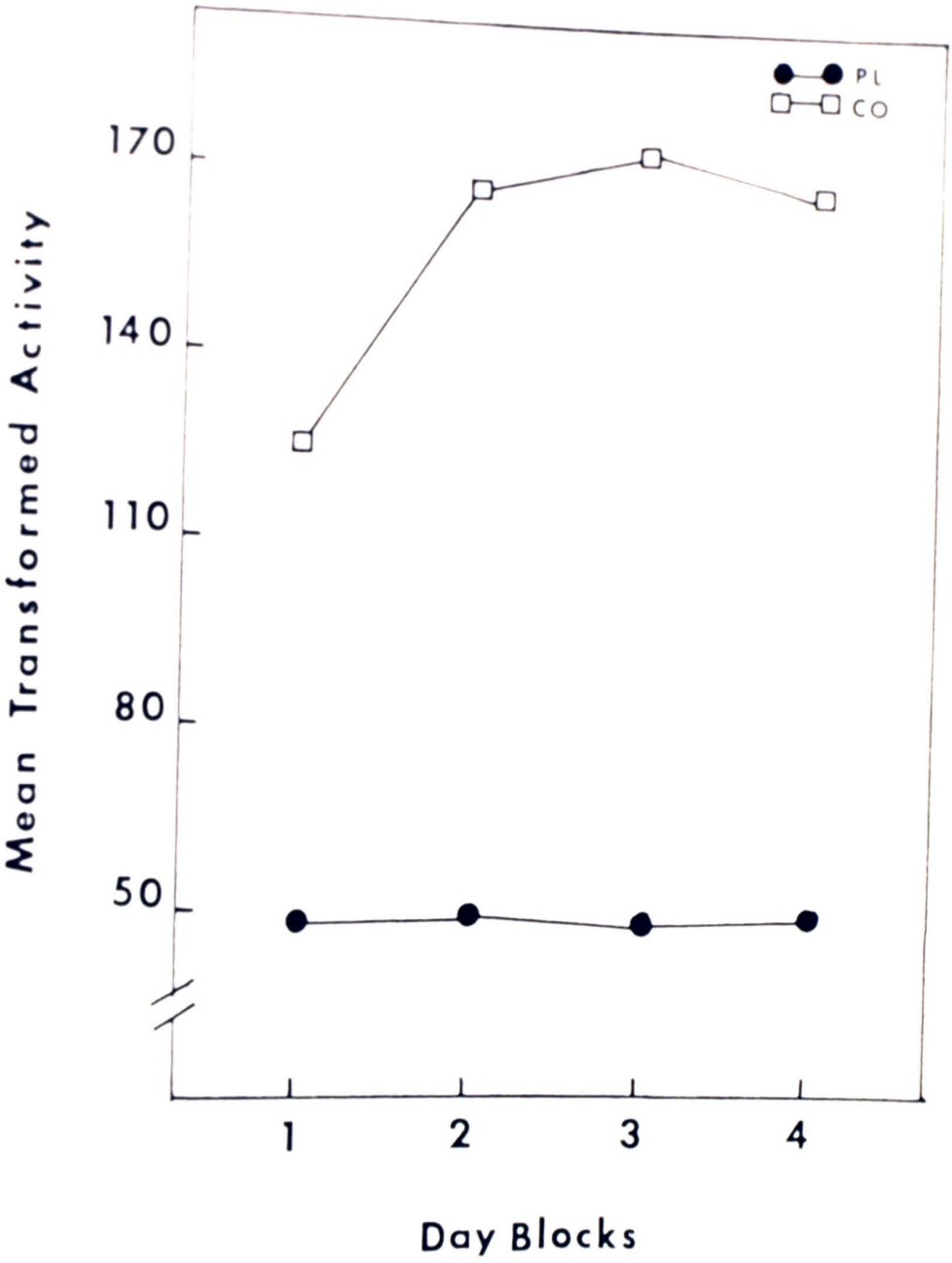

Mean Transformed Activity
115
110
105
100
95
Sound: Q N Q N
Start: Q N

the second block but remained constant throughout the rest of the study, DMR, $\alpha = .01$.

The rats in the cocaine group were more active than the rats in the placebo group, $F(1, 32) = 113.9$, $p<.001$. A significant interaction of drug with days was also obtained, $F(3, 96) = 22.4$, $p<.001$. While the activity levels of the cocaine group remained higher than those of the placebo group throughout the study, the activity levels of the rats receiving cocaine increased from the first to the second day block, DMR, $\alpha = .005$, (see Figure 7.). The activity levels of the placebo group, however, remained constant across all four 4 day blocks.

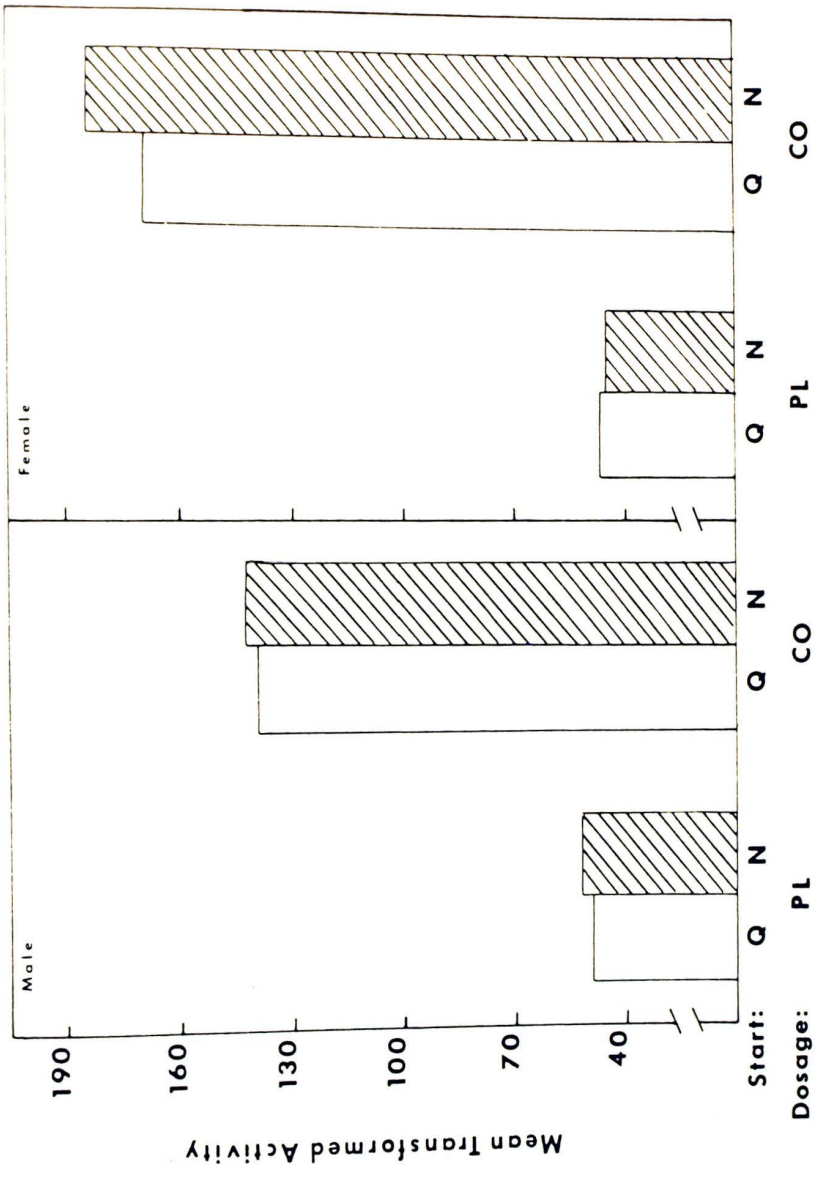
Cocaine dosage interacted significantly with starting condition, $F(1, 32) = 5.9$, $p<.05$, such that the rats receiving cocaine were significantly more active when the sessions started with the noise condition than when they started in the quiet, $F(1, 32) = 15.1$, $p<.005$, while the placebo group showed no difference between the two starting conditions, $F<1$. Gender also interacted significantly with the drug effects, $F(1, 32) = 4.5$, $p<.05$. Female rats in the cocaine group were more active than male rats in the cocaine group, while the two genders did not differ in the placebo group, DMR, $\alpha = .01$. This interaction, however, was not independent of starting condition, $F(1, 32) = 6.8$, $p<.05$. Simple effects analysis revealed that the female rats receiving cocaine were more active when started in the noise than in the quiet, $F(1, 32) = 20.1$, $p<.005$, while the male

Figure 7. Activity levels of the cocaine and placebo groups across the four day blocks.


PL
CO
170
140
110
80
50
Mean Transformed Activity
1
2
3
4
Day Blocks

rats receiving cocaine and all rats in the placebo group did not differ between the two starting conditions, $p>.05$, (see Figure 8).

Figure 8. Activity levels of the males and females in both drug groups under the two starting conditions.


Male
Female
190
160
130
100
70
40
Mean Transformed Activity
Start: Q N Q N Q N Q N
Dosage: PL CO PL CO

CHAPTER 6

Discussion

The results of Experiment 1 indicate that cocaine produces a dose related increase in locomotor activity. The activity levels of the rats were higher at the lowest dosage of cocaine (7.5 mg/kg) than at the placebo dosage and at the 15.0 mg/kg dosage activity levels were higher than at the low dosage. Activity levels at the 30 mg/kg dosage, however, were not significantly higher than those obtained at the 15 mg/kg dosage. The dose range employed in this study conforms approximately to that used in previous research (Scheel-Kruger et al. 1977). It is suggested from the findings in the present study that 15.0 mg/kg may be the optimum dosage for a locomotor activity measure and that 30.0 mg/kg may be too high.

A number of researchers have reported that cocaine produces short term increases in activity. It has also been reported to produce stereotypy when administered in high dosages. Scheel-Kruger et al. (1977) reported that the stimulant effects of cocaine were strong and reliable only when the animals were tested in a novel environment. The results of Experiment 1 seem to indicate, however, that cocaine produces an increase in activity in a relatively familiar environment.

Stimulant drugs other than cocaine, such as d-amphetamine and methylphenidate, have been shown to interact with ambient illumination (Alexander & Isaac, 1965; Golden & Isaac, 1977; Isaac & Troelstrup, 1969; Kallman & Isaac, 1975; Lowther & Isaac, 1976). These researchers have reported that the direction of the drug effect is dependent upon whether the animals under observation are nocturnal or diurnal. It also has been shown that the effects of these drugs are reduced under the dark condition regardless of the nocturnality or diurnality of the animals being tested (Golden & Isaac; Isaac & Troelstrup; Kallman & Isaac). Golden and Isaac reported obtaining a reduction in the activity levels of diurnal squirrel monkeys given d-amphetamine in both the light and the dark. However, the reduction was greater in the light than in the dark. These researchers suggested that this supports the hypothesis that the effects of d-amphetamine are similar to a reduction in ambient illumination (Golden & Isaac).

The results of Experiment 1 in the present study indicate that cocaine also interacts with ambient illumination. At the placebo and 7.5 mg/kg dosages, activity levels were higher in the dark than in the light. At the two higher dosages however, this relationship was reversed. Activity levels at the 15.0 and 30.0 mg/kg dosages were higher in the light than in the dark. Since rats are nocturnal and are usually more active in the dark than in the light and cocaine is a stimulant drug, this may

be an indication of overstimulation or overarousal. These data would appear to indicate that cocaine is unlike d-amphetamine and methylphenidate in its interaction with illumination.

The activity levels obtained with the 0.0 mg/kg dosage in Experiment 1 showed the decline in activity across intervals that has been reported by others (Delay, 1981; Wood, 1984). That is, activity levels were high at the beginning of the test session and declined significantly within the first thirty minutes of the test session. In the present study, activity levels at all three cocaine dosages in the first interval did not differ from each other but were higher than that obtained with the 0.0 mg/kg dosage. The difference between the activity levels at the three cocaine dosages was primarily one of duration of the activity response across the intervals. Activity under the low dosage of cocaine (7.5 mg/kg) showed a decline across the intervals similar to that seen with the 0.0 mg/kg dosage, although the levels of activity at this dosage remained somewhat higher than at the 0.0 mg/kg dosage. A decline in activity across the intervals did not occur under the two highest cocaine dosages (15.0 and 30.0 mg/kg). Activity levels at these two dosages remained high throughout the test session. At the 15 mg/kg dosage, activity declined slightly after the first interval and at the 30 mg/kg dosage there was little or no decline. After the first interval, the levels of activity at the 15.0 and

30.0 mg/kg dosages remained consistently high throughout the rest of the test session. Therefore, while all three dosages produced the same initial high levels of activity, the decline in activity levels at the three dosages across the intervals differed. Increasing dosages of cocaine produced slower rates of decline within the test sessions. It appears, therefore, that the dose effects of cocaine are not a function of increasing dosages producing higher levels of activity but rather that increasing dosages serve to increase the duration of high activity levels.

The results obtained on the data from the two non-drug days indicate that there continued to be a cocaine effect on the first day following injection. On the second day following injection, no significant dose effect was present. This indicates that there is a continuation of the cocaine effect until at least 24 hours following administration but not 48 hours following administration. On both non-drug days there was an illumination effect which was similar to the effect of illumination at the placebo and low dosage levels on the days that the cocaine was administered. That is, activity levels were higher in the dark than in the light. It is possible that, although there is a continuation of the cocaine effect through the first 24 hours following injection, the reversal of the illumination effect obtained at the two high dosages on the drug days is no longer present 24 hours following cocaine administration. Therefore, it is likely that this reversal of the

illumination effect on the cocaine administration days is dose dependent and that the drug's effects after 24 hours are no longer strong enough to produce it.

Unlike Experiment 1, in Experiment 2 the animals were tested in two groups, one receiving 15.0 mg/kg cocaine and the other receiving isotonic saline. The cocaine group was significantly more active than the placebo group. This supports the findings of Experiment 1 in that cocaine produced an increase in overall activity levels in both experiments. In Experiment 2, the cocaine group showed higher levels of activity in the second 4 day block than in the first and remained at that high level throughout the study. The placebo group on the other hand showed a much lower level of activity across all day blocks which remained constant throughout the study. It is likely that this represents habituation to the drug since the placebo group showed no change in activity across the day blocks and the drug group showed no further change after day block 2.

In general, activity levels were higher during the noise portions of the test sessions than in the quiet portions. Several other researchers have also reported increases in activity levels in the presence of masking noise (Delay, 1983; Seegal & Isaac, 1971; Wood, 1984). In the present study, however, overall activity levels were significantly greater when the masking noise was present only when the test session began in the noise. No noise effect was evident when the sessions started in the quiet.

This was the case even though the masking noise was introduced within 5 minutes of the start of these test sessions. It is possible then that the noise effect obtained in the present study as well as by other researchers occurs mainly in the first few minutes of the test session. Other researchers employing the noise variable have not employed the present technique of alternating noise conditions within sessions. Therefore further research using this technique is needed to determine more precisely the nature of the effects of masking noise on locomotor activity.

The results also indicate that cocaine interacted with both the starting condition and with gender. The female rats receiving cocaine were significantly more active when the test session began in the noise. However, male rats receiving cocaine and the placebo animals of both genders did not show a difference in overall activity levels between the two starting conditions. This is an interesting and unexpected finding. More research is needed to further examine gender related differences in the cocaine response.

The results of the present study indicate that cocaine has a stimulant effect on locomotor activity. The findings of Experiment 1 suggest that there are residual effects of cocaine present 24 but not 48 hours after administration. In addition, the effects of cocaine on activity levels appear to be a function of duration of effect rather than magnitude. No evidence of cocaine interference with

habituation was found. It appears, however, that the effects of the noise used to examine habituation may only be present during the early portion of the test sessions. A gender difference was also observed in the response to the drug and noise variables. Further research is needed in order to determine the nature of these findings.

APPENDIX

TABLE 1

Analysis of Variance for Experiment 1

Drug Days

SOURCE	SS	df	MS	F
TOTAL	194249.50	1919		
Between Groups	16960.85	19	892.67	
Sex (A)	4446.92	1	4446.92	6.39*
Error	12513.93	18	695.21	
Within Treatments	177288.65	1900	93.30	
Intervals (B)	33785.18	5	6757.03	174.68***
A x B	482.91	5	96.58	2.49*
Dose (C)	46779.47	3	15593.15	53.45***
A x C	2097.09	3	699.03	2.39
Illumination (D)	15.45	1	15.45	0.10
A x D	4.46	1	4.46	0.03
Replications (E)	3713.13	1	3713.13	14.77**
A x E	179.30	1	179.30	0.71
B x C	4535.99	15	302.39	11.71***
A x B x C	474.63	15	31.64	1.22
B x D	29.18	5	5.83	0.34
A x B x D	11.19	5	2.23	0.13
B x E	254.23	5	50.84	3.27**
A x B x E	219.02	5	43.80	2.82*
C x D	2022.41	3	674.13	3.40*
A x C x D	581.22	3	193.74	0.97
C x E	2160.45	3	720.15	6.18**
A x C x E	586.17	3	195.39	1.67
D x E	5.10	1	5.10	0.04
A x D x E	340.68	1	340.68	2.84

TABLE 1 (Continued)

SOURCE	SS	df	MS	F
B x C x D	524.27	15	34.95	1.94*
A x B x C x D	243.13	15	16.20	0.90
B x C x E	531.40	15	35.42	2.14**
A x B x C x E	165.73	15	11.04	0.67
B x D x E	114.22	5	22.84	1.20
A x B x D x E	142.11	5	28.42	1.49
C x D x E	356.27	3	118.75	1.27
A x C x D x E	329.75	3	109.91	1.17
B x C x D x E	177.05	15	11.80	0.69
A x B x C x D x E	307.77	15	20.51	1.21
Error	76119.55	1710	44.51	

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

TABLE 2

Analysis of Variance for Experiment 1

Non-Drug Day 1

SOURCE	SS	df	MS	F
TOTAL	92939.70	1919		
Between Groups	6438.46	19	338.86	
Sex (A)	43.78	1	43.78	0.12
Error	6394.68	18	355.26	
Within Treatments	86501.23	1900	45.52	
Intervals (B)	44755.46	5	8951.09	446.23***
A x B	250.02	5	50.00	2.49*
Dose (C)	593.33	3	197.77	9.85***
A x C	107.70	3	35.90	1.78
Illumination (D)	2341.83	1	2341.82	116.74***
A x D	291.56	1	291.56	14.53***
Replications (E)	177.33	1	177.33	8.84**
A x E	70.33	1	70.33	3.50
B x C	268.48	15	17.89	0.89
A x B x C	333.45	15	22.23	1.10
B x D	537.48	5	107.49	5.35*
A x B x D	45.76	5	9.15	0.45
B x E	404.15	5	80.83	20.14***
A x B x E	80.17	5	16.03	3.99
C x D	35.55	3	11.85	1.77
A x C x D	7.37	3	2.45	0.12
C x E	159.33	3	53.11	2.64
A x C x E	45.47	3	15.15	0.75
D x E	93.48	1	93.48	4.66*
A x D x E	4.38	1	4.38	0.21

TABLE 2 (Continued)

SOURCE	SS	df	MS	F
B x C x D	265.62	15	17.70	0.88
A x B x C x D	167.60	15	11.17	0.55
B x C x E	258.65	15	17.24	0.85
A x B x C x E	236.95	15	15.79	0.78
B x D x E	69.51	5	13.90	0.69
A x B x D x E	49.51	5	9.90	0.49
C x D x E	115.11	3	38.37	1.91
A x C x D x E	45.33	3	15.11	0.75
B x C x D x E	187.49	15	12.49	0.62
A x B x C x D x E	201.36	15	13.42	0.66
Error	34301.33	1710	20.05	

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

TABLE 3

Analysis of Variance for Experiment 1

Non-Drug Day 2

SOURCE	SS	df	MS	F
TOTAL	78977.61	1919		
Between Groups	5896.91	19	310.36	
Sex (A)	269.71	1	269.71	0.86
Error	5627.19	18	312.62	
Within Treatments	73080.70	1900	38.46	
Intervals (B)	35112.95	5	7022.59	374.88***
A x B	96.62	5	19.32	1.03
Dose (C)	74.50	3	24.83	1.32
A x C	83.22	3	27.74	1.48
Illumination (D)	2195.64	1	2195.64	117.20***
A x D	72.41	1	72.41	3.86*
Replications (E)	293.26	1	293.26	15.66***
A x E	17.70	1	17.70	0.94
B x C	251.73	15	16.78	0.89
A x B x C	154.09	15	10.27	0.54
B x D	448.72	5	89.74	4.79**
A x B x D	19.64	5	3.92	0.20
B x E	139.80	5	27.96	1.49
A x B x E	119.97	5	23.99	1.28
C x D	47.99	3	15.99	0.85
A x C x D	49.09	3	16.36	0.87
C x E	14.08	3	4.69	0.25
A x C x E	107.38	3	35.79	1.91
D x E	33.74	1	33.74	1.80
A x D x E	77.19	1	77.19	4.12*

TABLE 3 (Continued)

SOURCE	SS	df	MS	F
B x C x D	201.11	15	13.40	0.71
A x B x C x D	255.08	15	17.00	0.90
B x C x E	173.61	15	11.57	0.61
A x B x C x E	234.05	15	15.60	0.83
B x D x E	202.82	5	40.56	2.16
A x B x D x E	49.10	5	9.82	0.52
C x D x E	27.16	3	9.05	0.48
A x C x D x E	150.91	3	50.30	2.68*
B x C x D x E	184.29	15	12.28	0.65
A x B x C x D x E	160.01	15	10.66	0.77
Error	32032.70	1710	18.73	

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

TABLE 4

Analysis of Variance for Experiment 2

SOURCE	SS	df	MS	F
TOTAL	2700913.57	575		
Between Groups	2359135.50	35	67403.87	
Gender (A)	32805.11	1	32805.11	2.12
Drug (B)	1761892.11	1	1761892.11	113.94***
A x B	69639.27	1	69639.27	4.50*
Error	494799.00	32	15462.46	
Within Treatments	341778.06	540	632.92	
Sound (C)	6570.44	1	6570.44	8.44**
A x C	16.11	1	16.11	0.02
B x C	1602.02	1	1602.02	2.05
A x B x C	742.95	1	742.95	0.95
Error	24908.33	32	778.38	
Start (D)	4256.22	1	4256.22	9.35**
A x D	336.33	1	336.33	0.73
B x D	2708.58	1	2708.58	5.95*
A x B x D	3131.23	1	3131.23	6.88*
Error	14563.00	32	455.09	
Days (E)	56287.55	3	18762.51	24.55***
A x E	5412.44	3	1804.14	2.36
B x E	51351.09	3	17117.03	22.40***
A x B x E	4798.15	3	1599.38	2.09
Error	73353.42	96	764.09	
C x D	13272.11	1	13272.11	97.00***
A x C x D	49.05	1	49.05	0.35
B x C x D	257.69	1	257.69	1.88
A x B x C x D	0.00	1	0.00	0.00
Error	4378.41	32	136.82	
C x E	3285.50	3	1095.16	6.27***
A x C x E	303.69	3	101.23	0.58
B x C x E	469.10	3	156.36	0.89
A x B x C x E	50.90	3	16.96	0.09
Error	16757.27	96	174.55	

TABLE 4 (Continued)

SOURCE	SS	df	MS	F
D x E	4568.22	3	1522.74	4.16**
A x D x E	1570.58	3	523.52	1.43
B x D x E	1125.17	3	375.05	1.02
A x B x D x E	2242.61	3	747.53	2.04
Error	35101.21	96	365.63	
C x D x E	302.77	3	100.92	1.27
A x C x D x E	59.03	3	19.67	0.24
B x C x D x E	220.48	3	73.49	0.93
A x B x C x D x E	152.73	3	50.91	0.64
Error	7573.53	96	78.89	

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

REFERENCES

REFERENCES

Alexander, M., & Isaac, W. (1965). Effect of illumination and d-amphetamine on the activity of the rhesus macaque. Psychological Reports, 16, 311-313.

American Psychiatric Association. (1980). Diagnostic and statistics manual of mental disorders (3rd ed.). Washington, DC: Author.

Delay, E. (1981). Effects of illumination on activity following superior colliculus and caudate lesions in young and older rats. Physiology and Behavior, 27, 673-682.

Delay, E. (1985). Interactive effects of noise with illumination and age on activity of rats. Perceptual and Motor Skills, 60, 479-483.

Edwards, A. (1985). Experimental Design in Psychological Research (5th ed.). New York: Harper & Row.

Epstein, P., & Altshuler, H. (1978). Changes in the effects of cocaine during chronic treatment. Research Communications in Chemical Pathology, 22, 93-105.

Golden, A., & Isaac, W. (1977, May). Some effects of illumination and stimulant drugs on the activity of young and old squirrel monkeys of both sexes. Paper presented at the meeting of the Southeastern Psychological Association, Hollywood, FL.

Ho, B., Taylor, D., Estevez, V., Englert, L., & Mc Kenna, M. (1977). Behavioral effects of cocaine -- metabolic and neurochemical approach. In E. Ellinwood & M. Kilbey (Eds.), Cocaine and other stimulants (pp. 229-240). New York: Plenum Press.

Isaac, W., & Devito, J. (1958). Effect of sensory stimulation on the activity of normal and prefrontal-lobectomized monkeys. Journal of Comparative and Physiological Psychology, 51, 172-174.

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

Isaac W., & Reed, W. (1961). The effect of sensory stimulation on the activity of cats. Journal of Comparative and Physiological Psychology, 54, 677-678.

Isaac W., & Ruch, T. (1956). Evaluation of four activity techniques for monkeys. Science, 40, 313-318.

Kallman, W., & Isaac, W. (1975). The effects of age and illumination on the dose-response curves for three stimulants. Psychopharmacologia, 40, 313-318.

Kallman, W., & Isaac, W. (1977). Altering arousal in humans by varying sensory conditions. Perceptual and Motor Skills, 44, 19-22.

Lowther, W., & Isaac, W. (1976). The effects of d-amphetamine and illumination on behaviors of the squirrel monkey. Psychopharmacology, 50, 231-235.

Macphail, R., & Seiden, L. (1975). Time course for the effects of cocaine on fixed-ratio water-reinforced responding in rats. Psychopharmacologia, 44, 1-4.

Scheel-Kruger, J., Braestrup, C., Nielson, M., Golembiowska, K., Mogilnicka, E. (1977). Cocaine: Discussion on the role of dopamine in the biochemical mechanism of action. In E. Ellinwood & M. Kilbey (Eds.), Cocaine and other stimulants (pp. 373-407). New York: Plenum Press.

Van Dyke, C., & Byck, R. (1977). Cocaine: 1814-1974. In E. Ellinwood & M. Kilbey (Eds.), Cocaine and other stimulants (pp. 1-30). New York: Plenum Press.

Wallach, M., & Gershon, S. (1971). A neuropsychopharmacological comparison of d-amphetamine, l-dopa and cocaine. Neuropharmacology, 10, 743-752.

Wood, M. (1984, March). The effects of varying intensities of pulsed masking noise on weanling rats. Paper presented at the meeting of the Southeastern Psychological Association, New Orleans, LA.