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Pharmacological Effects on Aggression and Manual Responding Generated by Tail Shock in the Squirrel Monkey

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PHARMACOLOGICAL EFFECTS ON AGGRESSION AND MANUAL RESPONDING GENERATED BY TAIL SHOCK IN THE SQUIRREL MONKEY

by

Grace S. Emley

A dissertation submitted to the Faculty of The Graduate College in partial fulfillment of the Degree of Doctor of Philosophy

Western Michigan University
Kalamazoo, Michigan
December 1978
The response-independent, fixed-time delivery of electric tail shock in the squirrel monkey generated bites on a rubber hose immediately following shock delivery and manual responses on a lever immediately preceding shock. The procedure generated two temporally and topographically different responses in the single organism in a single experimental session. All responses were measured objectively via response manipulanda and recorded on cumulative recorders and counters. Nine pharmacological compounds were administered to the squirrel monkey after a stable baseline of bite and lever press responding had been established. Three stimulant compounds - d-amphetamine, caffeine, cocaine; three tranquilizer compounds - nicotine, chlordiazepoxide, chlorpromazine; and three sedative compounds - alcohol, phenobarbital, and morphine were administered on this baseline. The stimulant compounds had the general effect of elevating both responses; the tranquilizer compounds had the general effect of elevating lever press responding while depressing bite responding across a portion of the dosage range; the sedative compounds had the general effect of depressing both responses. Each compound had a differential effect on the response and a complete dose response function was obtained for each subject on each compound. The procedure appears to be a good one for testing behavioral effects of drugs. The responses are contingency free so that the effect of a drug cannot be to alter any response produced environmental consequences. The recording
of two separate responses from one organism in a single experimental session allows for the measurement of selective and differential drug effects. The squirrel monkey subject is ideal also because it is a primate and close to the human in drug dosage ranges which enables the possibility of generalizing to the human.
ACKNOWLEDGEMENTS

I would like to thank my committee members, Dr. Frederick P. Gault, Dr. David O. Lyon, Dr. Paul T. Mountjoy and Dr. Leonard J. Beuving for their interest and advice in this project. The assistance of the personnel of the Research Department and The Foundation for Behavioral Research in the conducting of these experiments and of Ms. Susan Dickerman in typing the manuscript are greatly appreciated. Especial thanks to my husband, Dr. Ronald R. Hutchinson for his continuing support and encouragement throughout this project.

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Grace S. Emley
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WESTERN MICHIGAN UNIVERSITY, PH.D., 1978

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INTRODUCTION

Aggression and attack performances have been shown to result from two major classes of environmental variables (Hutchinson, 1973). Certain types of antecedent environmental stimulation can directly produce instances of aggression (Ulrich and Azrin, 1962; Azrin, Hutchinson and Hake, 1963) while other types of stimulation occurring subsequent to aggression will also increase its future likelihood (Azrin and Hutchinson, 1967). Two types of antecedent environmental stimulation produce attack. The occurrence or instatement of noxious, painful, aversive or negative-reinforcing stimulation will lead directly to aggression and attack sequences (Ulrich and Azrin, 1962; Azrin et al., 1963; Azrin, Hutchinson and Sallery, 1964; Azrin, Hake and Hutchinson, 1965). Alternatively, removal or withholding of pleasant, beneficial, biologically necessary, or positively-reinforcing stimuli produce aggression sequences directly (Azrin, Hutchinson and Hake, 1966; Hutchinson, Azrin and Hunt, 1968).

Aggressive behavior can be generated by the application of electric shock, intense heat, or a physical blow (Tedeschi, Tedeschi, Mucha, Cook, Mattis and Fellows, 1959; Ulrich and Azrin, 1962; Azrin et al., 1965). Electric shock elicited fighting behavior has been studied in several species including monkey (Azrin et al., 1963; Hutchinson, 1973), cats (Ulrich, Wolff and Azrin, 1964), hamster and rat (O'Kelly and Steckle, 1939; Ulrich and Azrin, 1962) and mouse (Tedeschi et al., 1959). Fighting behavior can also be induced by isolation (Yen, Stanger and Millman, 1958; DaVanzo, Daugherty, Ruckart.
and Kang, 1966). Early laboratory studies (O'Kelly and Steckle, 1939; Daniel, 1943) investigated fighting behavior in groups of subjects. Electric shock applied to the grid floor of an experimental chamber generated fighting behavior between two naive subjects. This fighting behavior occurred immediately after the delivery of foot shock. Many studies were done by Azrin, Hutchinson and Ulrich to determine the parameters under which fighting behavior occurred. Subsequent to these studies procedures were developed for studying attack by the solitary subject against an inanimate object (Hutchinson, Azrin and Hake, 1966; Azrin, Rubin and Hutchinson, 1968). The single organism procedures in which the subject bites an inanimate object such as a tennis ball or rubber hose provide an objective and reliable recording of the aggressive response by an electric switch closure instead of the visual recording and reporting by an observer of fighting behavior in paired subjects. Additionally, attack responses in these studies are not influenced by injury to a subject or threat of counter-attack.

The shock-elicited aggression procedure developed for measuring bite attack in the squirrel monkey provides a sensitive and reliable measure of frequency, intensity, and duration of attack responses in the single organism. The frequency of biting a rubber hose in response to a brief electric tail shock (Hutchinson et al., 1966) is a direct function of intensity and duration of shock (Hutchinson, Azrin and Renfrew, 1968) with the highest frequency of biting occurring immediately after shock presentation. These aggression sequences can be produced by originally neutral stimuli (tone or light) once these
stimuli have been associated with unconditional attack eliciting (shock) conditions (Hutchinson et al., 1971). For example, if a tone or light is presented before the shock occurrence and is terminated with the shock offset, the tone or light will, over time, become associated with the shock and produce a response similar to that elicited by the shock. The tone or light which were originally neutral become conditioned stimuli which elicit conditioned responses. In further work, however, it has been shown that other types of behavioral reaction sequences are prepotent over attack sequences during occurrence of conditional stimulation. During conditional stimulation prior to actual occurrence of attack eliciting stimulation, locomotor, manual, and visual scanning reaction topographies are observed and replace attack reactions (Hutchinson et al., 1971; Hutchinson and Emley, 1972; Hutchinson, 1977). These manipulative reactions are pre-potent over attack sequences prior to the instatement of unconditional-attack-eliciting-stimuli while attack sequences occur following onset of such stimulation. This pattern of behaviors is maintained even though no reinforcement through stimulus termination, reduction or delay occurs. The objective recording of shock-induced aggressive and manipulative behavior in a single primate organism permits the investigation of the influence of other variables on aggressive behavior.

Since one of the principal clinical applications of psychotropic drugs is in altering reactivity to aversive stimulation, i.e., to reduce tension and anxiety, a procedure for measuring reactions to aversive stimulation in the primate in a controlled laboratory setting seemed optimal for testing such drugs.
The effects of psychotropic drugs have been studied by many investigators on several experimental models of aggressive behaviors. These models of aggressive behavior include (1) handling or taming procedure, (2) isolation-induced aggression, (3) footshock-induced aggression in paired subjects, (4) extinction-induced aggression, and (5) interspecies aggression. Drug effects in these models will be reviewed.

The handling procedure (Scheckel and Boff, 1966) in which squirrel monkeys are used measures attacks on the hand of the experimenter during attempts to handle the monkey in the home cage. Taming effects of the drugged monkey are determined as attempts to bite when prodded, poked or handled by the experimenter.

Isolation-induced aggression (DaVanzo et al., 1966; Valzelli, 1967; Welch and Welch, 1969) procedures involve housing mice in isolation for approximately 21 days and then introducing an intruder non-isolated mouse into the cage with the isolated mouse. The number of fighting episodes and fighting time are recorded for five minutes following introduction of the intruder mouse. Footshock-induced fighting in paired rats (Lai, Defeo and Thut, 1968; Crowley, 1972; Powell, Walters, Duncan and Holley, 1973; Eichelman, Orenberg, Hackley and Barchas, 1978) and mice (Tedeschi et al., 1959) is another procedure for testing drug effects on aggression. The paired animals are placed on a grid floor in an enclosure and shock is delivered to the grid floor for a period of approximately three minutes. Drug is administered to both subjects and number of fights in the three-minute period is used as the measure of aggression.
Two additional models of elicited aggression involve (1) extinction-induced aggression in which subjects responding on a regular reinforcement schedule for food or water are placed on extinction and responses on a target object are elicited, and (2) exposing a male Siamese fighting fish to a male con-specific eliciting stimulus.

The effects of drugs on aggression can be divided by general classification of the drugs tested. Stimulant, tranquilizer, and depressant type drugs have been studied on several different models of aggressive behavior. Effects of the several stimulant (amphetamine, cocaine, caffeine) tranquilizer [nicotine, (Geller and Hartmann, 1969) chlordiazepoxide, chlorpromazine] and depressant (alcohol, phenobarbital, morphine) drugs studied in this experiment will be reviewed.

The effects of stimulants on aggressive behavior are varied but when wide ranges of dosages are tested there is a biphasic effect of increases at low dosages and decreases at high dosages. d-Amphetamine had no effect on aggressiveness in the squirrel monkey in the range of dosages tested (0.05 - 0.5 mg/kg p.o.) for taming by Scheckel and Boff (1966).

In studies of isolation-induced aggression in the mouse subject, d-amphetamine has been shown to (1) decrease aggression only at dosages that produced signs of neurotoxicity (DaVanzo et al., 1966), (2) produce no inhibition in fighting at dosages tested (5 mg/kg i.p.) (Valzelli, 1967), or (3) produce a biphasic effect of increases in aggression at low doses and decreases at high dosages (Welch and Welch, 1969; Miczek and O'Donnell, 1978).
On footshock elicitation of fighting in paired mice, Tedeschi, Fowler, Miller and Macko (1969) observed a slight increase in fighting at 2.5 mg/kg (i.p.) d-amphetamine but a decrease in fighting at 5.0 mg/kg (i.p.). In paired rat subjects, Lal et al. (1968) report a decrease in aggression at 3 mg/kg (i.p.) amphetamine, whereas Powell et al. (1973) report essentially no effect across a range of from 0.5 to 5 mg/kg (s.c.). Crowley (1972) testing methamphetamine in this same procedure, reports an increase in fighting in dosages up to 1 mg/kg (i.p.) and then decreases at higher dosages. The fact that several investigators testing a range of dosages found a biphasic effect seems to indicate that the dosage tested is a critical feature of these investigations.

Caffeine has been shown to have an antiaggressive effect in isolated mice at low dosages followed by a hyperexcitation effect at high dosages (10 - 20 mg/kg i.p.) (Valzelli and Bernasconi, 1973). Eichelman et al. (1978) studied the effects of caffeine on footshock-induced fighting in paired rats and reported an increase in fighting across the dosage range (25 - 150 mg/kg i.p.) tested. Quenzer, Feldman and Moore (1974) reported an anti-aggression effect of caffeine on shock-induced fighting in paired rats. However, differences in shock parameters may be responsible for these discrepancies.

Moore and Thompson (1978) report no effect at low dosages and decreased extinction-induced aggression responding at high dosages of cocaine in the pigeon.

The general effect of tranquilizers is to decrease aggressive behavior and in cases in which general activity was measured to depress
activity as well. Chlordiazepoxide had a taming effect on the squirrel monkey such that aggressiveness was selectively depressed and general motor activity (measured by Sidman avoidance) was not affected (Scheckel and Boff, 1966). Beattie, Barry and Lister (1970) report a decrease in aggression toward a human intruder in baboons given chlordiazepoxide or chlorpromazine. Porsolt and Loew (1974) report a decrease in shock elicited biting behavior in the squirrel monkey.


The sedative or depressant drugs generally decrease aggressive behavior. Krsiak (1976) reports a biphasic effect of ethanol in isolation-induced attack by mouse subjects. Miczek and Barry (1977) also report a biphasic effect of alcohol on fighting behavior of rat subjects. Alcohol tested on the display response of the fighting fish
resulted in a facilitation of aggressive responding at low dosages and a decrease at higher dosages (Raynes, Ryback and Ingle, 1968).

Similarly to chlorpromazine, phenobarbital produced no taming effect in the procedure by Scheckel and Boff (1966). In procedures of isolation-induced fighting phenobarbital had no selective effects on fighting and reduced all behaviors at sedative doses (Janssen et al., 1960; Yen et al., 1959; DaVanzo et al., 1966). Tedeschi et al. (1959) and Chen et al. (1963) reported no effects on footshock-induced fighting in paired mice until a sedative dose was administered. Randall (1961) reported a selective decrease in fighting at doses below the muscle relaxant dose for paired mice. Crowley (1972) reported a biphasic effect of phenobarbital on paired rats. Fight time and number of episodes were increased at low dosages while general activity and fight time were depressed at high (80 mg/kg i.p.) doses.

Morphine has been reported to depress fighting and motor activity in isolated mice (Janssen et al., 1960; DaVanzo et al., 1966) and to increase aggressiveness in the fighting fish (Walaszek and Abood, 1956).

This procedure of the present study was selected because it provided a reliable and objective measure of aggression in a single organism and the simultaneous measure of a temporally and topographically separate response. The recording of two separate responses allowed for the determination of selective drug effects not possible in other procedures. The present study used the shock-elicited aggression procedure in the squirrel monkey to test several psychotropic drugs. This study determined the effects of nine drugs (three from each—stimulant, tranquilizer and depressant classes) on the aggression and manual
manipulative reactions recorded from the primate in a single exper­
mental session. The data are compared to effects of these drugs on
other behavioral procedures to determine if the drug effects were
specific to the class of behaviors generated by this experimental pro­
cedure and to determine if the procedure is a useful one for testing
behavioral effects of drugs.
METHOD

Subjects

The subjects were 22 squirrel monkeys (Saimiri sciureus), 18 males (MP-12, MC-20, MC-1, MP-13, M-273, MD-3, MC-3, MC-13, MC-16, MC-19, MC-5, MC-12, MC-82, MC-84, MC-81, MC-70, MC-76, MC-50) weighing between 700 and 950 grams and 4 females (MC-26, MC-27, MC-28, MC-29) weighing 575 to 675 grams. Subjects were housed in individual cages in a large colony room providing illumination, temperature, and humidity control. Subjects had free access to water in the home cage and were fed Wayne Monkey Diet.

Apparatus

Primate restraint chairs (Plas Labs Mfg., Lansing, Michigan) equipped with tail electrodes (Hake and Azrin, 1963) were used during these experiments. The subject was restrained at the waist with the tail held in a stockade device. The brass electrodes rested on the tail. A latex rubber bite hose was mounted on the removable front panel of the chair, 18 cm up from the waist lock and 5 cm in front of the monkey (Figure 1). The hose was connected to an Air Wave switch (Tapeswitch Corp., Farmingdale, New York) which was calibrated to record only bite attacks. Compression of the hose by the teeth caused the air flow switch to trigger. Grasping, tugging, squeezing or shaking the hose with hands or arms had no effect on the switch. A response lever (LVE #1352, Lehigh Valley Electronics, Fogelsvill, PA) which required 20 grams of force for a response to be recorded was mounted.
Figure 1. A squirrel monkey seated in the restraint chair. The bite hose is indicated by the letter A. The response lever on the intelligence panel is indicated by the letter B. The tail electrodes through which the electric shock was delivered is indicated by the letter C.
on the intelligence panel. The restraint chair was enclosed in an outer chamber providing sound attenuation and ventilation. The chamber was illuminated by four three watt light bulbs and masking noise (84 db) was provided by a white noise generator. Hose bites and lever presses were recorded on cumulative recorders and counters located in an adjoining room.

**Procedure**

During each 64 minute session, 15 electric tail shocks (200 msec, 400 v ac) were delivered on a 4 minute fixed-time, response-independent schedule. Shock was delivered through a 50 K ohm resistor to the brass tail electrodes. The distal portion of the tail which fit under the electrodes was shaved, cleansed with alcohol and prepared with electrode paste prior to each session. Experimental sessions were conducted 5 days a week. Baseline conditions were continued for at least 2 months prior to drug administration.

**Drug Administration**

The drugs administered, route of administration, and the pretreatment times are indicated in Table I.

Drugs given subcutaneously were prepared in physiological saline and injected in a constant volume of 0.5 cc. Drugs were administered in a mixed order of dosages on Wednesday of a five day experimental week. Drug administrations were separated by at least four experimental sessions. Saline control injections were given on these four days. Alcohol was given intraperitoneally and was prepared in physiological saline to a 30% v/v concentration and injected in different volumes.
Table I. Summary table of drugs administered, number of subjects for each drug, route of administration, pretreatment time and number of dosages administered.
**TABLE I**

<table>
<thead>
<tr>
<th>Drug</th>
<th>N</th>
<th>Route</th>
<th>Pretreatment Time</th>
<th># Dosages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dextro Amphetamine Sulfate</td>
<td>5</td>
<td>s.c.</td>
<td>30 minute</td>
<td>6</td>
</tr>
<tr>
<td>Caffeine and Sodium Benzoate</td>
<td>4</td>
<td>s.c.</td>
<td>30 minute</td>
<td>8</td>
</tr>
<tr>
<td>Cocaine Hydrochloride</td>
<td>6</td>
<td>s.c.</td>
<td>30 minute</td>
<td>7</td>
</tr>
<tr>
<td>Nicotine Tartrate</td>
<td>4</td>
<td>s.c.</td>
<td>5 minute</td>
<td>8</td>
</tr>
<tr>
<td>Chlordiazepoxide Hydrochloride</td>
<td>5</td>
<td>s.c.</td>
<td>30 minute</td>
<td>8*(11)</td>
</tr>
<tr>
<td>Chlorpromazine Hydrochloride</td>
<td>6</td>
<td>s.c.</td>
<td>30 minute</td>
<td>6</td>
</tr>
<tr>
<td>Ethyl Alcohol</td>
<td>6</td>
<td>i.p.</td>
<td>30 minute</td>
<td>6</td>
</tr>
<tr>
<td>Phenobarbital</td>
<td>4</td>
<td>s.c.</td>
<td>60 minute</td>
<td>9</td>
</tr>
<tr>
<td>Morphine Sulfate</td>
<td>4</td>
<td>s.c.</td>
<td>30 minute</td>
<td>6</td>
</tr>
</tbody>
</table>

* One animal, MD-3, received 11 dosages of this compound.
depending upon the dosage desired. Control intraperitoneal injections were given weekly. The range of dosages tested on each animal was determined by the response to the drug. An attempt was made to find the range of minimal to maximal effect for each drug for each subject. Therefore, the dosage ranges were not constant from subject to subject. Most subjects were tested on more than one drug, therefore, the 22 monkey subjects resulted in a total of 44 drug subjects. Behavioral measures from a minimum of one month of saline control baseline were obtained before a new drug regimen was initiated.
RESULTS

The presentation of response independent tail shocks on a four-minute fixed-time schedule generated a control pattern of responding illustrated in Figure 2. Biting attack on the rubber hose occurred immediately after the shock while lever pressing occurred prior to the shock. For several seconds immediately prior to the shock there was an absence or reduction of bite and lever press behavior. These behaviors were not shaped or conditioned in any conventional manner and all animals did not show exactly the same behaviors. Therefore, control baselines for some subjects might represent only lever pressing or biting while other subjects might exhibit both biting and lever pressing.

These behaviors were modified by the administration of various drugs. Figure 3 is a composite of the effects of all nine compounds tested in this experiment. The data presented are expressed as the percent change in responses at each dosage point as determined by comparing the saline control for the immediately preceding four days and the drug response at each dosage for all subjects receiving that dosage. The stimulant drugs (d-amphetamine, caffeine, and cocaine) at intermediate dosages had the effect of increasing both classes of responses while at high dosages they decreased biting behavior before lever pressing. The tranquilizer type drugs (nicotine, chlordiazepoxide, and chlorpromazine) at low to intermediate dosages had the effect of differentially elevating lever pressing behavior while they reduced biting behavior. The sedative drugs (alcohol, phenobarbital,
Figure 2. Sample cumulative records from one squirrel monkey subject. The lower record is cumulative lever press responses and the top record is cumulative bite responses for one control session.
Figure 3. The effect of nine compounds on fixed-time, response-independent shock produced bite and lever press responses in the squirrel monkey. Solid circles represent bites and open circles represent lever presses. The line at zero is the average of the immediately preceding saline control days. Bite and lever press points are presented as the percent change from the immediately preceding saline control for each drug dosage. N is the number of subjects given a particular compound.
d-AMPHETAMINE

CAFFEINE

N=4

COCaine

N=5

N=6

NICOTINE

N=4

CHLORDIAZEPoxide

N=5

CHLORPROMAZINE

N=6

ALCOHOL

N=6

PHENOBARBITAL

N=4

MORPHINE

N=4

PERCENT CHANGE

DOSAGE

mg./kg.

mg./kg.
and morphine) had the effect of decreasing both behaviors although decreasing lever pressing behavior more than biting. The figure also illustrates the dose response function for each drug.

Table II presents the results of the Wilcoxon Signed Ranks test applied to the data in Figure 3. This analysis indicates the dosage in which responding under drug is significantly different from saline control and the direction of the difference from control. All of the differences, whether increases or decreases, are significant except the effect of chlorpromazine on bite responses and the effect of chlordiazepoxide on lever press responses.

Figures 4 through 12 are illustrations for each drug showing the complete data for all subjects. The data presented are expressed as the percent change from the saline control for the immediately preceding four days for bites and lever presses. Each individual graph illustrates the particular dose response function for an individual subject. Therefore, dosage ranges may vary slightly from subject to subject as well as magnitude of response at each dosage.

Figure 4 shows the results for the five subjects receiving d-amphetamine. All subjects showed an inverted U function with an increase in both behaviors across a range of dosages and a decrease in both behaviors at the higher dosages. Biting behavior was increased more than lever pressing behavior with the exception of the high increases in lever pressing for MC-20 and MP-13. These large increases are due to the low number of responses on control and in the case of MP-13, the absence of lever pressing on control. All subjects showed similar effects of the drug on biting and lever pressing across a
Table II. The results of the Wilcoxon Signed Ranks test indicating the level and direction of significant differences from saline control levels for bite and lever press responses.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Range (mg/kg)</th>
<th>n</th>
<th>Bites Sig.</th>
<th>Direction</th>
<th>n</th>
<th>Lever Press Sig.</th>
<th>Direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>d-amphetamine</td>
<td>0.125 - 1</td>
<td>5</td>
<td>&lt; .01</td>
<td>increase</td>
<td>5</td>
<td>&lt; .02</td>
<td>increase</td>
</tr>
<tr>
<td>caffeine</td>
<td>0.06 - 10</td>
<td>4</td>
<td>&lt; .01</td>
<td>increase</td>
<td>2</td>
<td>&lt; .01</td>
<td>increase</td>
</tr>
<tr>
<td>cocaine</td>
<td>0.06 - 1.75</td>
<td>5</td>
<td>&lt; .01</td>
<td>increase</td>
<td>5</td>
<td>&lt; .01</td>
<td>increase</td>
</tr>
<tr>
<td>nicotine</td>
<td>0.16 - 0.8</td>
<td>4*</td>
<td>&gt; .05</td>
<td>decrease</td>
<td>4</td>
<td>&lt; .02</td>
<td>increase</td>
</tr>
<tr>
<td>chlordiazepoxide</td>
<td>1.0 - 16</td>
<td>5</td>
<td>&lt; .01</td>
<td>decrease</td>
<td>3</td>
<td>&gt; .05</td>
<td>increase</td>
</tr>
<tr>
<td>chlorpromazine</td>
<td>0.25 - 2</td>
<td>6</td>
<td>&lt; .01</td>
<td>decrease</td>
<td>6</td>
<td>&lt; .05</td>
<td>increase</td>
</tr>
<tr>
<td></td>
<td>0.06 - 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>alcohol</td>
<td>250 - 1200</td>
<td>5</td>
<td>&lt; .02</td>
<td>decrease</td>
<td>6</td>
<td>&lt; .02</td>
<td>decrease</td>
</tr>
<tr>
<td>phenobarbital</td>
<td>.5 - 20</td>
<td>4</td>
<td>&lt; .05</td>
<td>decrease</td>
<td>2</td>
<td>&lt; .05</td>
<td>decrease</td>
</tr>
<tr>
<td>morphine</td>
<td>0.06 - 2</td>
<td>4</td>
<td>&lt; .01</td>
<td>decrease</td>
<td>3</td>
<td>&lt; .01</td>
<td>decrease</td>
</tr>
</tbody>
</table>

* n=3 p < .05 (MP-13 omitted from analysis)
Figure 4. Results for five subjects given d-amphetamine. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
d - AMPHETAMINE

LEVER PRESSES

BITES

PERCENT CHANGE

MC-26

MC-20

MC-1

MP-13

.06 .125 .25 .5 1.0 2.0

mg/kg

DOSAGE

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The decreases at the high dosages do not indicate a total lack of responding but rather an absence of responding on the manipulandum provided.

Figure 5 illustrates the results for the four subjects receiving caffeine. Two subjects (M-273, M-29) had biting and lever pressing responses on control sessions, two subjects (MD-3, MP-13) had only biting behavior on control conditions. For three subjects all responses were elevated across the range of dosages tested. Lever pressing and pre-shock biting (MP-13) were elevated more than post-shock biting. The data for MP-13 are presented in two forms. The graph in the middle of the lower portion of the figure illustrates total bite responses, but because pre-shock biting responses appear only under drug the lower left graph separates post-shock bites and pre-shock bites. The high percent changes in this behavior are a result of the absence of this behavior on control sessions. The pre-shock biting behavior was affected by the drug in a manner similar to pre-shock lever pressing.

One subject, MD-3, was an exceptionally non-responsive animal in this procedure, and showed essentially no effect of the drug across the dosage range tested. It was necessary in later tests to use very high dosages of morphine, phenobarbital and chlordiazepoxide to obtain response modification with this animal, suggesting that this animal may have responded to higher dosages of caffeine also if they had been given.

The data for the five subjects tested with cocaine are illustrated in Figure 6. All subjects had lever press and bite responses on control
Figure 5. Results for four subjects given caffeine. Data are presented as percent change from immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
Figure 6. Results for the five subjects given cocaine. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
COCAINONE

LEVER PRESSES

BITES

BITES BEFORE SHOCK

BITES AFTER SHOCK

MC-70

MC-76

MC-50

MC-84

MC-81

MC-81

CHANGE

PERCENT

0 100 200 300 400 500

0 100 200 300 400 500

0 100 200 300 400 500

0 100 200 300 400 500

0 100 200 300 400 500

0 100 200 300 400 500

118 112

221 24

102 32

643 35

275 96

0 100 200 300

0 100 200 300

0 100 200 300

0 100 200 300

0 100 200 300

0.5 25 75 125 1.5

0.5 25 75 125 1.5

0.5 25 75 125 1.5

0.5 25 75 125 1.5

0.5 25 75 125 1.5

mg/kg

mg/kg

mg/kg

DOSAGE
conditions and responding was elevated across the dosage range tested with a decrease in both behaviors at the highest dosages. For each subject there was a range of dosages for which lever press responses were elevated more than biting responses. In the case of MC-81, in which both behaviors were elevated similarly across the dosage range, pre-shock biting responses occurred and are separated from the post-shock biting responses. When pre- and post-shock biting responses are graphed the dose response function was similar to the post-shock biting and pre-shock lever pressing of the other subjects.

Figure 7 illustrates the results for four subjects on nicotine. Three subjects (MC-1, MC-26, MP-12) had biting and lever pressing control baselines. Subject MP-13 again, as previously on d-amphetamine and caffeine, had only biting on control. Therefore, for this analysis with MP-13, pre-shock and post-shock biting responses are separated. For each subject at low and intermediate dosages of nicotine the biting behavior was reduced or unaffected while the lever pressing behavior was elevated. This relationship is illustrated for pre- and post-shock biting for MP-13. For three of the four animals, all behavior was elevated at the higher dosages of the drug.

The data for the five subjects on chlordiazepoxide are illustrated in Figure 8. Three subjects (MC-29, MC-28, MC-3) had bite and lever press control baselines. Each of these subjects showed an increase in lever pressing and a dose dependent decrease in biting behavior over much of the dosage range. Lever pressing for MC-28 was unchanged or relatively less depressed than biting across the dosage range tested. MC-3 exhibited bite responses on control and was relatively unresponsive.
Figure 7. Results for four subjects given nicotine. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
Figure 8. Results for five subjects given chlordiazepoxide. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
to this drug as was the case when the same subject was tested on caffeine (Figure 5). At a dosage of 80 mg/kg, more than twice the highest dose given to the other subjects, there was a slight increase in bite responses and several lever presses were emitted. The lever presses occurred only under the drug condition so the percent increase is very large.

Figure 9 illustrates the results for the six subjects receiving chlorpromazine. Four of these subjects (MC-29, MC-20, MC-3, MC-26) had lever press and bite responses on control conditions. Subjects MC-29, MC-20 and MC-3 each showed a dose dependent decrease in bite responses and an elevation in lever pressing across the range of dosages tested with a decrease in both behaviors at the highest dosages. Subject MC-26 had pre-shock biting behavior on control conditions such that a pre-, post-shock biting analysis was made and in this analysis the pre-shock biting was elevated relative to the post-shock biting. Subjects MC-16 and MC-1 had no lever press responses on baseline but these responses did occur at several dosages of drug. When pre- and post-shock bite responses are separated for these subjects, an elevation of pre-shock bites relative to post-shock bites is seen throughout most of the dosage range with both responses being depressed at the highest dosage.

Figure 10 shows the data for six subjects given alcohol. Both MC-29 and MC-12 show a dose dependent decrease in both responses with lever presses being more depressed than biting. Subject MC-1 showed an atypical stimulation of lever press behavior and little effect on biting at the dosage range tested. Subjects MC-27 and MP-13 did not
Figure 9. Results for six subjects given chlorpromazine. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage point are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
Figure 10. Results of six subjects given alcohol. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
have both bites and lever presses in the same session but in the absence of the hose would respond on the lever before shock. For these two subjects, the bite hose was removed from the chamber on alternate weeks such that drug was administered on either a bite or a lever press baseline. Subject MC-27 exhibited a dose dependent decrease in both responses, and MP-13 showed a slight elevation in lever presses at the lowest dosage but generally little effect or a slight dose dependent decrease in responses.

Subject MC-5 had only lever press responses before shock and no responses after shock. This lever press responding showed a dose dependent decrease except at the highest dosage tested.

The data for phenobarbital are illustrated in Figure 11. Both M-273 and MC-29 showed bite and lever press baselines and both showed a dose dependent decrease in both behaviors. The lever press responding was depressed relatively more than the bite responding. Subject MC-12 did not exhibit lever press responding and showed a dose dependent decrease in bite responding. As was the case when given caffeine and chlordiazepoxide, MD-3 was essentially unresponsive in this procedure to the dosages of phenobarbital tested. There was a minimal response at 40 mg/kg but the animal was too sedated at 60 mg/kg to be run in the experimental procedure.

Figure 12 shows the data for the four subjects given morphine. Subjects MC-3, MC-13 and MP-12 had bite and lever press control baselines. All of these subjects showed a dose dependent decrease in both responses, although lever press responses were relatively more depressed than bite responses. Subject MC-3 showed a stimulation
Figure 11. Results for four subjects given phenobarbital. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
Figure 12. Results for four subjects given morphine. Data are presented as percent change from the immediately preceding saline control average. Each point represents one experimental session. Data points at each dosage are from the same experimental session. The numbers on the zero line represent the average number of lever press and bite responses on all control days.
effect of lever presses at a dose of .25 mg/kg. This dosage was repeated with the same effect each time. Similarly, the stimulation effect on bites for MC-13 at .125 mg/kg was also replicated. Subject MD-3 had only bite baseline and was relatively unaffected by the drug until the highest dosages. For morphine the decreases in behavior were greater than those produced by alcohol or phenobarbital.

Figure 13 presents sections of cumulative records for control and drug responding for one subject (MC-29) in a single session under a drug from each of the three classes of drugs tested; caffeine, a stimulant; chlordiazepoxide, a tranquilizer; and phenobarbital, a sedative or depressant. In each case, the control record is shown under the drug record and bite records are on the left and lever press records on the right. The section of each pair of records (lever press and bite) is from the same time segment within the session. The dosage showing maximum typical effect was chosen for each drug. In the case of caffeine, the records show that both lever press and bite responding were elevated over control while for chlordiazepoxide lever press responding was increased while bite responding was decreased. The records also show both responses were depressed under phenobarbital.
Figure 13. Segments of cumulative records of lever presses and bites during control and drug sessions for one subject. The top pair of records illustrate a saline control and a caffeine session. The middle pair of records illustrate a saline control and a chlordiazepoxide session. The bottom records illustrate a control and a phenobarbital session.
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DISCUSSION

The results of this experiment on the effects of several pharmacological compounds on aggressive and manual manipulative responding in the squirrel monkey indicate that each of the drugs tested had a differential effect on the responses measured and the general behavioral effects resulted in the division of the drugs into three general categories. The categorization of each drug by behavioral effect generally agrees with the pharmacological categorization of these drugs. The general elevation of both biting and lever pressing responses across a major part of the dosage range is produced by d-amphetamine, caffeine and cocaine, all stimulant compounds. The elevation of the lever pressing response with the simultaneous depression of the biting response is produced by nicotine, chlordiazepoxide and chlorpromazine, all tranquilizer-type compounds. Finally, the general depressant effect on both responses is produced by alcohol, phenobarbital and morphine, all sedative compounds. This general categorization indicates that the effects produced by this method do not conflict with the generally accepted pharmacological effects of these drugs. However, the responses produced by this method are selectively affected by each compound and allow differentiation between compounds.

d-Amphetamine produces a biphasic effect on both responses across the dosage range tested. The increase in aggressive responding occurs at lower dosages than does the elevation of lever pressing, while both
responses are depressed at the high end of the dose response function. The dose dependent biphasic effect of amphetamine on aggressive responding has been reported previously by other investigators (Tedeschi et al., 1969; Welch and Welch, 1969; Crowley, 1972; Miczek and O'Donnell, 1978). The selective effect of amphetamine on responding in this experiment is similar to that reported in other procedures in which locomotor activity is measured in addition to aggression. Tedeschi et al. (1969) reported increases in locomotor activity in mice at a dose of amphetamine at which aggressive behavior was decreased; however, because of the selection of only two dose levels, this study provides an incomplete picture of the effects of amphetamine on fighting and locomotor activity. Additionally, Tedeschi et al. (1969) measured locomotor activity at a time and place separate from the measurement of fighting behavior. Crowley (1972) reported effects of methamphetamine on electric shock-induced fighting in rats and measured locomotor activity in the same chamber at the same time. The results of this experiment (Figure 1, p. 217) are similar to the selective effect of amphetamine noted in the present study. Crowley (1972) reported an increase in fight time and activity at low doses with a depression in fight time at high doses while activity was still elevated.

Caffeine produces an increase in both biting and lever pressing responses. This drug elevates lever press responding more than biting across the range of dosages tested, while at the high end of the dosage range, both behaviors are elevated. Data previously reported on effects of caffeine on aggression are very confusing. Valzelli and
Bernasconi (1973) reported an antiaggressive effect of caffeine on isolated mice, however, hyperexcitation was reported at the higher dosages. Since intensity of aggressiveness was measured on a scale from 0 to 100 and all saline control intensities were rated at 100, increases in aggression produced by caffeine would not be elevated higher than saline control. Therefore, the evaluation system used does not allow for measurement of increases over saline control levels of aggressiveness. In two other studies (Eichelman et al., 1978; Quenzer et al., 1974), experimental methods differ markedly such that caffeine results cannot be compared. Hyperexcitation and general stimulation have been noted previously with high dosages of caffeine (Gilbert, 1976).

The cocaine effects, though similar to other stimulant effects, show a biphasic effect on biting but a general elevating effect on lever pressing. Miczek and O'Donnell (1975) reported an increase in fighting behavior in the mouse at low doses followed by decreases in fighting.

The effect of nicotine in this experiment was to elevate lever press responses and depress or leave unchanged bite responses across the low to intermediate dosages and to elevate both behaviors at the higher dosages. Silverman (1969) reported that a "smoking dose" of nicotine administered to paired rats reduced aggression while increasing tendency to escape. This report presented only one dosage level.

Chlordiazepoxide at low to intermediate doses depressed aggressive responding while leaving unchanged or slightly elevating lever press responses. At the high doses bite responses were reduced more
than lever press responses. In a study by Christmas and Maxwell (1970) chlordiazepoxide depressed aggression in mice and rats while at the same dosage, increased ambulation in an open field test. The majority of studies with chlordiazepoxide indicate an antiaggression effect at doses that also produce neurotoxic side effects.

Chlorpromazine increases lever press responding at low doses and produces no change or a slight decrement at the higher dosages. Bite responses on the other hand are elevated at low dosages and depressed at the higher dosages. Previous work of other investigators report a nonselective depression of aggression responding.

Alcohol produces relatively no change or a slight increase in aggression until a depression at the highest dosage tested while there is a dose-dependent decrease in lever press responding. The biphasic effect of alcohol on aggressive responding has been reported by other investigators (Krsiak, 1976; Miczek and Barry, 1977).

Phenobarbital has a slight elevating effect on biting at the lowest dosages followed by a dose-dependent decrease in aggression responses. The lever press behavior shows a similar effect with a much greater dose-dependent decrement across the dosage range tested to a total absence of bite and lever press responding at the highest dosage. A similar differentiation was noted by Crowley (1972) on shock-induced fighting in rat pairs. A dose-dependent decrease in fight time and activity were reported with the decrement in activity being greater (Figure 2, p. 217).

Morphine produces a dose-dependent decrement in both responses with the lever press response decrement being greater until both

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responses are essentially absent at the highest dosages. The stimulant effect at one low dose (.125 mg/kg) could be a general stimulation effect but these are usually noted at high doses (Jaffe, 1976). However, McMillan and Morse (1967) have demonstrated elevations of key pecking in pigeons at low dosages of morphine and Ayhan and Randrup (1973) report increased locomotor activity in the rat at low doses of morphine.

A general fundamental principle of pharmacology is that drugs have multiple and complex effects and therefore resist classification into single categories. The results of this experiment indicate that the behavioral effects of several drugs divide them into general categories but within each category each drug has its own specific and selective effects on the responses measured. Additionally, drugs have different effects at different dosages, so to establish the range of effects of a drug it is necessary to determine an effective dose response function. The present experiment provides this information for the drugs tested and the responses measured. Previous studies have reported on only portions of the dose response function and thus reported only part of the effects of the compounds. The individual dose response functions presented illustrate the individual differences between subjects as well as the similarity among subjects. The overall effects of the drug are similar for each subject tested although the dose response function may be shifted slightly to the upper or lower end of the dosage scale. The comparison of the effects of three different drugs on one experimental subject is important since it demonstrates that the differential and selective effects of the
three different classes of drugs can be produced in a single subject.

Behavioral effects of drugs are often analyzed in terms of the ongoing or baseline rate of responding. The rate dependency hypothesis states that the principal determinant of behavioral effects is the ongoing rate of responding such that the way in which a drug modifies behavior is quantitatively related to the level of responding before the drug was given. Dews (1958) studying the effects of methamphetamine on fixed-interval and fixed-ratio performance of pigeons suggested that the effects of drugs depend critically on the type of schedule. The rate dependency hypothesis developed out of this work and stated that the effect of amphetamine on responding is dependent on pre-drug rate of responding as well as drug dosages. High rates of responding will be progressively reduced by increasing doses of amphetamine whereas low rates of responding will be progressively elevated by increasing doses of amphetamine. Subsequently, similar effects have been reported for the benzodiazepines (Wuttke and Kelleher, 1970), barbiturates (McKearney, 1970) and morphine (Thompson, Trombley, Luke and Lott, 1970).

The fact that actions of many drugs can be quantitatively related in an increase linear function to pre-drug rates does not imply that all behavioral effects can be interpreted as rate dependencies (Kelleher and Morse, 1968). Sanger and Blackman (1976) cite many studies that support the rate dependent hypothesis for amphetamine and also cite exceptions to this hypothesis. There are three types of responding which to date are considered exceptions to this hypothesis: (1) responding under strong stimulus control; (2) responding maintained at
very low rates by stimuli associated with electric shock (punishment and conditioned suppression); (3) responding that has not previously occurred or has no programmed consequences. The issue of rate of responding is critical to this theory. Kelleher and Morse (1968) refer to high rates as rates of responding greater than one response per second and low rates as rates less than one response per second. In graphs and data presentations in these studies rates of 2-10 responses per minute are often presented. Rate of responding is a function of many variables and schedules of reinforcement which produce different rates of responding and also produce many other differences such as frequencies of reinforcement, patterning of responding, pausing, nature of response, and stimulus control. In rate analysis studies, schedules of reinforcement are used which generate different rates of responding as well as different frequencies of reinforcement. When frequency of reinforcement is held constant and high and low response rates generated, Thompson and Corr (1974) found that d-amphetamine effects were not clearly rate-dependent and Sanger and Blackman (1975) found rate-dependent effects for amphetamine but not chlordiazepoxide. Verhave (1958) studied effects of methamphetamine on responding that has no programmed consequence and found that four of six subjects did not respond at all after drug administration regardless of pre-drug rate.

Data from the present experiment do not fit into an analysis based on the rate dependency hypothesis for several reasons: (1) the responding has no programmed consequence and (2) the amount of responding per session is lower than the rates of responding typically generated
by schedules of reinforcement and subjected to rate analysis. The rates of bite and lever press responding vary from subject to subject both in absolute and relative terms although drug effects of the two responses are consistent across subjects. Glick and Muller (1971) also report a dose dependent inverted U-shaped function for amphetamine on FR (fixed-ratio) responding and prandial drinking in rats independent of baseline rate. If the rate dependency hypothesis fit it would be expected that drug effects would be dependent on baseline rates of responding. This is clearly not true of the data of this experiment. Behavioral effects tend to be in terms of type of drug rather than baseline rate of responding.

The results of this experiment confirm several previous reports of drug effects on aggressive responding. Additionally, they provide complete dose response functions for the compounds tested and provide information on a separate and simultaneous behavior such that a distinction can be made between general sedation and selective effects on aggressive responding. Because there are two separate response topographies drugs can effect both responses similarly or differentially, increase, decrease, or leave unchanged, one or both responses. The lever press response generated by the response independent fixed time delivery of shock in this experiment is not only a measure of general activity but resembles an escape-avoidant type response which occurs during the last portion of the intershock interval. The lever press probability is greatest about one to one and a half minutes prior to shock, and this response is prepotent over the bite response during this portion of the intershock interval. For the few seconds immediately
prior to shock there is an absence of behavior or a freeze reaction. The lever press response has been described previously by Hutchinson et al. (1971) as an escape/avoidance type reaction. As with the bite attack response in this procedure, there are no environmental consequences of the lever press, yet it occurs regularly and reliably from session to session. Other responses occur during the same time period as the lever press but were not objectively measured or recorded in this study. Since these lever press or manual responses occur during the time period prior to the onset of unconditional shock stimuli, there may be some conditioning processes such that this behavior becomes conditioned. In the experimental literature, the behaviors that are similar to this lever press response are few but the effect of drugs on behaviors in response to aversive stimulation may be relevant. The procedures involving such behaviors include avoidance, escape, punishment, conflict and conditioned suppression.

The bite and lever press responses of the present experiment though consequence free may be similar in motivation to other responses studied by other investigators. The bite response is a sensitive and valid index of more naturalistic attack reactions studied by others. The lever press, anticipatory manipulative responding seems to be an index of escape or flight tendency and has temporal characteristics of avoidance performances. Therefore, it is important to compare results of the present experiment with results of other investigators on similar response measures.

In avoidance responding which is responding to conditioned stimuli and escape responding which is responding to unconditional stimulation,
Boren (1961) has found that chlorpromazine decreases avoidance responding but not escape. Heise (1965) reported that chlorpromazine and phenobarbital depressed avoidance responding. Cook and Kelleher (1962) reported that chlorpromazine and morphine block avoidance at doses that leave escape responding intact whereas phenobarbital produced a nonspecific block of avoidance responding. Cook and Catania (1964) also reported that chlorpromazine suppressed avoidance but not escape. Dantzer (1977) reported that chlordiazepoxide blocks both avoidance and escape responding, and Davis and Kensler (1973) in an experiment with squirrel monkeys reported an increase in continuous avoidance with nicotine, d-amphetamine and caffeine. Since both avoidance and escape responses have environmental consequences relative to the shock these responses are not the same as the lever press response in the present experiment. The drug effects on the avoidance and escape reactions reported are similar to the reactions of increases in lever press responses for nicotine, d-amphetamine, and caffeine and the differential depression of lever press and bite responding for morphine. However, the actions of chlorpromazine, chlordiazepoxide and phenobarbital of increasing one response while decreasing the other or leaving one unchanged while simultaneously changing the other cannot be explained by the previously reported effects on avoidance and escape reactions. In punishment procedures in which responses produce the delivery of electric shock, Dinsmoor and Lyon (1961) reported a selective effect of chlorpromazine on punished behavior and Blum (1970) reported that chlordiazepoxide attenuates punished responding. Woods (1977) reported
that cocaine elevates behavior suppressed by punishment. Sepinwall, Grodsky and Cook (1978) reported a dose dependent increase by chlor diazepoxide on punished behavior. These results are similar to the results of various drugs on lever press responding in the present experiment but the lever press in the present experiment does not produce the delivery of electric shock.

The conditioned suppression procedure in which a stimulus precedes the delivery of an unavoidable shock is another place to look for responding similar to the lever press measure of the present experiment. Hill, Bell and dikler (1967) reported that morphine reduced suppression or increased responding during the tone preceding shock. Boren (1961) reported the monkeys used in this study on conditioned suppression developed agitated behaviors during the warning stimulus. These behaviors consisted of jumping, rocking and shaking. Chlorpromazine was not effective in reducing the avoidance lever pressing or the agitation reactions during the warning stimulus although all reactions were reduced at general sedative doses. Millenson and Leslie (1974) presented a review of the effects of phenothiazines, benzodiazepines and barbiturates on conditioned suppression responding. The data are variable and their review of many studies indicated that all the drugs were effective in reducing the conditioned emotional response on some set of conditions. Houser and Cash (1975) in a similar procedure superimposed a CS followed by unavoidable shock on an avoidance schedule. Bar pressing was increased during the CS and they observed that if bar pressing was not increased it was because the monkey was attempting to escape and was directing its activity.
toward clawing the door or engaging in other non-recorded activity. This observation in addition to that of Boren indicates that a lot of escape or flight type activity does take place during the stimulus period preceding an unavoidable shock.

Several investigators have attempted to measure activity levels in addition to avoidance and aggression responding. Tedeschi et al. (1969) used a photocell counter device to record activity of mice and found that chlorpromazine depressed both fighting and activity, and phenobarbital depressed all behaviors only at sedative levels. Yen et al. (1959) observed physical activity including hyperactivity, excitability and jumping during the isolation-induced fighting episodes and reported that chlorpromazine depressed both behaviors while phenobarbital had no effect on either behavior. Janssen et al. (1960) reported activity in terms of the righting reflex, reactions on a hot plate and coordinated motor activity on a rotating rod. Morphine reduced aggression and motor activity and phenobarbital and chlorpromazine depressed all behavior. Crowley (1972) used a light beam in the chamber to record activity of paired rats; methamphetamine increased the motor activity of the subjects such that fighting was decreased. Phenobarbital increased activity at low dosages and suppressed both fighting and activity at high dosages.

The measurement of general activity reported by other investigators involved the observation by an experimenter or measures of reactions that took place in conjunction with or in separate time and places from the aggression responding. The lever press responding in the present study is reliable, objectively recorded and is available.
in the same environment as the attack response, yet it does not interfere or have any time or physical components the same as the attack response. Clearly, the reports of Boren (1961) and Houser and Cash (1975) indicated that such manipulative, sensory scanning reactions occur during the period preceding an unavoidable shock; however, the present study allows these responses to occur in an environment completely devoid of contingent responding such that the drug effect is not altering several aspects of the environment simultaneously. The ability to record two temporally and topographically separate responses in a single organism in a single environmental session in one experimental chamber without the interference of contingency control is an important power of this experimental procedure.

The advantages of this experimental procedure for measuring aggression are many when compared with other experimental models of aggression. In contrast to footshock-induced aggression in paired subjects, there is no second subject so problems of threat of counter attack or injury are avoided. Additionally, the direct delivery of shock to a restrained subject is more reliable than shock delivery through floor grids upon which the subject has the freedom of movement and through postural shifts can alter and reduce shock intensity. In contrast to isolation-induced aggression in which subjects that fight are selected, the response-independent shock procedure generates stable daily rates of biting which can be maintained for long periods without debilitating effects. The single subject procedure additionally is objective and free of experimenter bias and interobserver reliability considerations. The use of the squirrel monkey subject is an additional
advantage of this procedure. Previous investigators have indicated the desirability of using the squirrel monkey in research (Uyeno, 1975; Kelleher, Gill, Riddle and Cook, 1963). Hanson (1968) has provided information on the squirrel monkey which indicated the similarity of effective drug dosages between the squirrel monkey and the human. Clearly, the dosages used in this experiment are considerably different from the drug dosages used with the mouse or rat subject and much closer to the human drug dosage.
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