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Contrasting Effects of *d*-Amphetamine on Affiliation and Aggression in Monkeys

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SMITH, E. O. AND L. D. BYRD. *Contrasting effects of d-amphetamine on affiliation and aggression in monkeys.* PHARMACOL BIOCHEM BEHAV 20(2) 255–260, 1984.—Amphetamine has been observed to alter conditioned or learned behavior in individually housed animals, as well as naturally-occurring behavior characteristic of animals living in groups. This study is concerned with the effects of *d*-amphetamine on affiliative and aggressive behavior in adult male stumptail macaques *(Macaca arctoides)* living in a large, heterogeneous social group. Using standardized observational techniques, the affiliative and aggressive behaviors initiated by five adult male monkeys were characterized and quantitated in the absence of and following drug administration. Acute administration of a range of doses of *d*-amphetamine (0.003–0.56 mg/kg) resulted in a monotonically depressive effect on the rate of affiliative behavior initiated by the experimental animals. In contrast, *d*-amphetamine increased the rate of aggressive behavior initiated by the highest- and lowest-ranking monkeys, and had little or no effect in the mid-ranking monkeys. These results show that *d*-amphetamine can have qualitatively different effects on affiliative and aggressive behavior in the same subjects. The results also provide evidence that the effects of *d*-amphetamine can be determined by the hierarchical or dominance position of the subject in the group.

d-Amphetamine *Macaca arctoides* Affiliative behavior Aggressive behavior

AMPHETAMINE can produce orderly changes in conditioned or learned behavior in a variety of species [6,8]. Several reports have indicated that amphetamine can also alter naturally-occurring behaviors characteristic of animals in groups [2, 10, 11, 12, 25]. Typically, experiments of the former type have been conducted in individual subjects isolated from other animals in the environment, whereas the latter type have been conducted in small groups of animals housed together in a large cage or a room.

Commonalities between these two areas of research are not well defined nor is the appropriateness of predicting from one to the other area well documented. Indeed, whereas a given effect may occur independently of species, sex, age or size of the subject when studying conditioned behavior in an isolated animal, the same does not appear to pertain when studying naturally-occurring behaviors in individual members of a group. Utena *et al.* [25] studied methamphetamine in group-living macaques, for example, and reported that amphetamine-induced changes in aggressive behavior were a function of the dominance position of the subject in the group. In contrast, the effects on grooming, a non-aggressive behavior, were similar across animals of various ranks.

These results suggest that amphetamine can have contrasting effects on different, naturally-occurring behaviors and that the effects may depend on the type of behavior studied and on factors related to the hierarchical arrangement of animals in the group. The present report describes a study conducted with a large, stable group of monkeys to obtain definitive data on the relation among the effects of *d*-amphetamine and behaviors characteristic of members of the group, the relation between the effects and drug dose, and changes in effects over time. Because aggression is at the opposite end of the behavioral spectrum from affiliation, these two types of behavior were chosen to test the hypothesis that the effects of *d*-amphetamine can covary with the type of behavior and with the dominance position of the individual subject in the group.

METHOD

Subjects

The experimental subjects were five adult male stumptail macaques *(Macaca arctoides)*, weighing between 13.8 kg and 22.9 kg, and ranging in age from 5 to 11.5 years. The five subjects lived in a heterogeneous group of 37 animals that included five adult males, 18 adult females, three subadult females, three juvenile males, two juvenile females and six immatures. The group of 37 animals was confined within a 28.4×32.7 m outdoor enclosure or compound and an adjacent environmentally-controlled indoor area (4.4×12.2 m) that was accessible via two metal tunnels [24]. The positions of the five male subjects within the dominance hierarchy of the group ranged from the highest- to the lowest-ranking.

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TABLE 1
TYPICAL BEHAVIORS COMPRISING AFFILIATION AND AGGRESSION

Name	Definition
	Affiliation
Groom	Spreading the hair of another and removing debris by hand or mouth.
Contact	Any nonspecific contact between two animals.
Huddle	Extensive body contact with some weight support; does not include holding another animal.
Hold	Grip or hold onto part of another's body.
Touch	Placement of hand or fingers on another with minimal pressure.
	Aggression
Open mouth threat	Mouth corners are partially retracted; mouth is not widely open; some teeth show.
Displace	Moving into another's place.
Chase	Movement toward another who is fleeing.
Bite	To make contact with teeth so as to wound another.
Hit	Striking another with hand(s).

Procedures

All animals were restricted to the outdoor compound on a prescribed daily schedule, weather permitting. While in the compound, each member of the group could be observed from a tower located 4.27 m above one side. Data characterizing the behavior of individual animals were collected and stored in a digital format using a microprocessor-based data collection device, the Datamyte 900 [23]. Subjects were observed and data recorded during 15-minute test periods at pre-selected post-injection times using the focal-animal technique described by Altmann [1]. The focal animal sampling technique allows for the recording of all occurrences of various behaviors of an individual monkey during each sampling period. In this manner, a descriptive record can be obtained of the focal animal's behavior and of its interactions with others in the group. In the present experiment, changes in aggressive and affiliative behaviors following the administration of *d*-amphetamine were studied. Affiliative behaviors were defined as any positive or affectionate behavior, or any behavior which was an attempt to safeguard another animal. Aggressive behaviors were operationally defined as those behaviors which could cause physical injury, signal the potential for harm or result in preferential access to objects and events in the environment (Table 1).

The positions of individual animals in the dominance hierarchy were determined and verified based on the outcome of agonistic encounters among members of the group under baseline or non-drug conditions. An independent measure of dominance ranking was also obtained which involved scoring priority of access to a preferred food item (orange halves). Correlations between rankings based on the outcome of agonistic encounters and displacement over preferred food items were high (r_s=0.96). Dominance rankings of the males in the group have been determined and have been recorded weekly since the animals were initially released into the outdoor enclosure in December, 1979.

To study changes in aggressive and affiliative behaviors as a consequence of *d*-amphetamine administration, the drug was dissolved in sterile normal saline (0.9%) and injected intramuscularly in a volume of less than 1.0 ml. Sodium chloride solution (0.9%) served as a control (placebo) injection. Except for the highest dose (0.56 mg/kg) studied in monkey M-13 and the lowest dose (0.003 mg/kg) studied in monkey M-18, each dose was studied three times in each subject in an unsystematic order.

In order to administer injections without alarming or exciting the animals, each of the five male subjects was trained to enter a small cubicle along one side of the outdoor compound [22] and to extend an arm through a circular opening according to procedures devised previously for chimpanzees [3,4]. On a given day, each of the five subjects would receive either a drug injection, a saline (placebo) injection or no injection; however, only the experimental animal for that day would receive the drug. Those personnel responsible for data collection did not know whether saline or drug was administered. *d*-Amphetamine was administered two days per week, but a given animal was the experimental or drug subject no more than once per week. Immediately after completing the injections, the five male subjects returned to the compound and data collection began. The initial observation period encompassed the entire first hour post-injection; thereafter, 15-minute periods of observation were scheduled at 90, 150, 210 and 330 minutes post-injection. For each experimental subject, aggressive and affiliative behaviors initiated by that subject were scored.

RESULTS

Mean hourly rates of occurrence of affiliative behavior and aggressive behavior were determined for each subject following drug or saline administration based on observations during the period 90–180 minutes post-injection. Under saline or control conditions, affiliative behavior initiated by each of the five subjects was characterized by rates ranging between 20–50 occurrences per hour. The highest-ranking subject in the dominance hierarchy (M-13) had a low control rate of affiliative behavior, and the lowest-ranking subjects (M-18 and M-24) had relatively high control rates (Fig. 1). Following the administration of a wide range of doses of *d*-amphetampne (0.003–0.56 mg/kg), four of the five subjects showed a dose-related decrease in the rate of affiliative behavior. The lower doses produced little effect, and doses of 0.3–0.56 mg/kg decreased rates markedly. Moreover, the initiation of affiliative behavior was affected similarly in the high-ranking and low-ranking subjects, and there was no discernible evidence of differential effect among those monkeys. The only subject in which *d*-amphetamine did not produce a pronounced decrease in rate of affiliative behavior was monkey M-06, a mid-ranking animal.

A more detailed analysis of the effects of *d*-amphetamine on affiliative behavior revealed that the drug affected the various individual behaviors comprising affiliation by decreasing the rate of occurrence of each. The most pronounced decrease was evident in the rate of grooming, the most common type of affiliative behavior, and the least pronounced decrease was characteristic of touching behav-

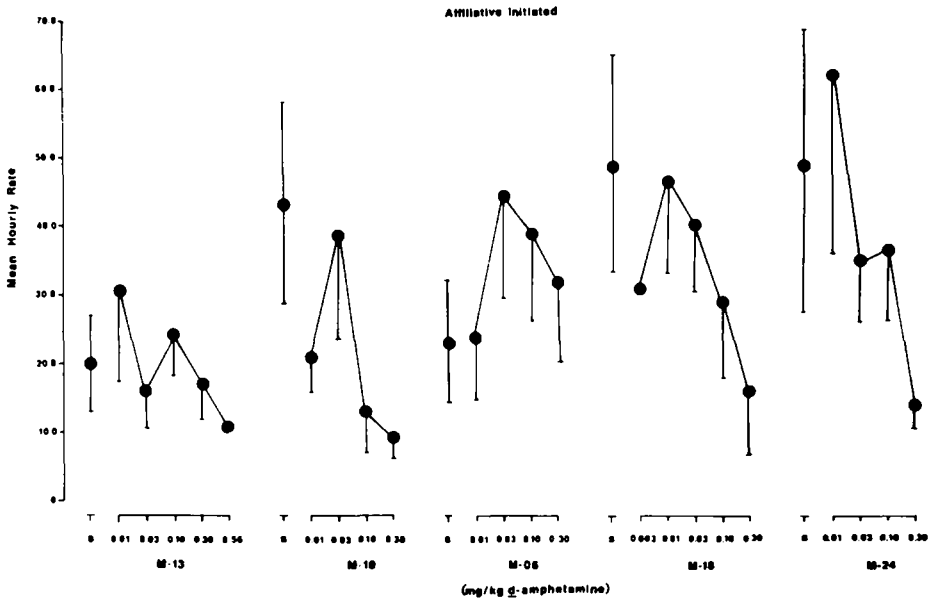

FIG. 1. Effect of *d*-amphetamine on rate of affiliative behavior in five adult male stumptail macaques. Each data point is the mean±SEM based on three administrations (except that the highest dose for M-13 and the lowest dose for M-18 are based on only one administration). Data points to the left of the dose-effect curves were obtained when saline was administered as a control.

ior (Table 2). The magnitude of change in individual types of affiliative behavior varied among the five subjects.

In contrast to the monotonically depressive effect of *d*-amphetamine on affiliative behavior, the drug markedly increased the rate of aggressive behavior in the same monkeys. *d*-Amphetamine increased the rate of aggressive behavior initiated by the highest- and lowest-ranking monkeys and had little or no effect in the two mid-ranking subjects at the doses studied (Fig. 2). The largest increase in rate was observed in monkey M-13, the highest-ranking animal in the group. Rate in that monkey increased in direct relation to increases in dose, and at the highest dose studied (0.56 mg/kg), rate increased more to than 30 times the saline values. *d*-Amphetamine also increased the rate of aggressive behavior initiated by monkeys M-18 and M-24, the two lowest-ranking subjects, with a dose of 0.003 mg/kg having no effect and intermediate doses (0.01–0.03 mg/kg) increasing rate two- to eight-fold over rates observed in the absence of the drug. A dose of 0.3 mg/kg produced decreases in rate in the two low-ranking monkeys, and the resulting dose-effect curves conformed to inverted U-shaped functions (Fig. 2). There was no change in the rate of aggressive behavior over the same range of doses of *d*-amphetamine (0.01–0.3 mg/kg) in monkeys M-10 and M-06, the two mid-ranking subjects in the group. Their behavioral rates remained in the range of rates observed in the absence of the drug, i.e., when saline was administered.

Qualitative differences in the effects of *d*-amphetamine on affiliative and aggressive behavior in individual subjects were also apparent when drug effects were plotted as a function of time since injection. Figure 3 presents time-course curves for monkey M-18 when either 0.01 or 0.3 mg/kg was administered. The former dose resulted in the greatest increase in aggressive behavior in this monkey and the latter produced the greatest decrease in affiliative behavior. Maximum effects on aggressive behavior in this and other monkeys were obtained during the period 90–180 minutes post-injection.

TABLE 2

EFFECTS OF 0.3 mg/kg *d*-AMPHETAMINE ON THE FREQUENCY OF INITIATION OF AFFILIATIVE BEHAVIORS BY INDIVIDUAL SUBJECTS*

Subject†	Groom	Contact	Huddle	Hold	Touch
M-13	1.33 (1.33)	4.67 (7.33)	0.00 (0.67)	1.33 (0.00)	0.00 (0.67)
M-10	1.50 (10.67)	1.00 (4.67)	0.00 (0.00)	0.00 (2.67)	0.00 (0.67)
M-06	0.00 (1.33)	6.67 (4.67)	0.00 (0.00)	0.00 (0.00)	1.33 (1.33)
M-18	0.00 (10.67)	0.00 (4.00)	0.00 (10.67)	0.00 (0.00)	0.00 (0.00)
M-24	0.50 (17.33)	1.00 (2.67)	0.00 (0.67)	0.00 (0.67)	0.50 (0.67)
Total	3.33 (41.33)	13.34 (23.34)	0.00 (12.01)	1.33 (3.34)	1.83 (3.34)

*The data are mean hourly rates during 90–180 min post-injection for five types of affiliative behavior. Comparable saline (control) values are shown in parentheses.

†Subjects are listed in descending hierarchical rank.

DISCUSSION

The present data show that *d*-amphetamine can have qualitatively contrasting effects on different classes of naturally-occurring behavior in individual monkeys compris-

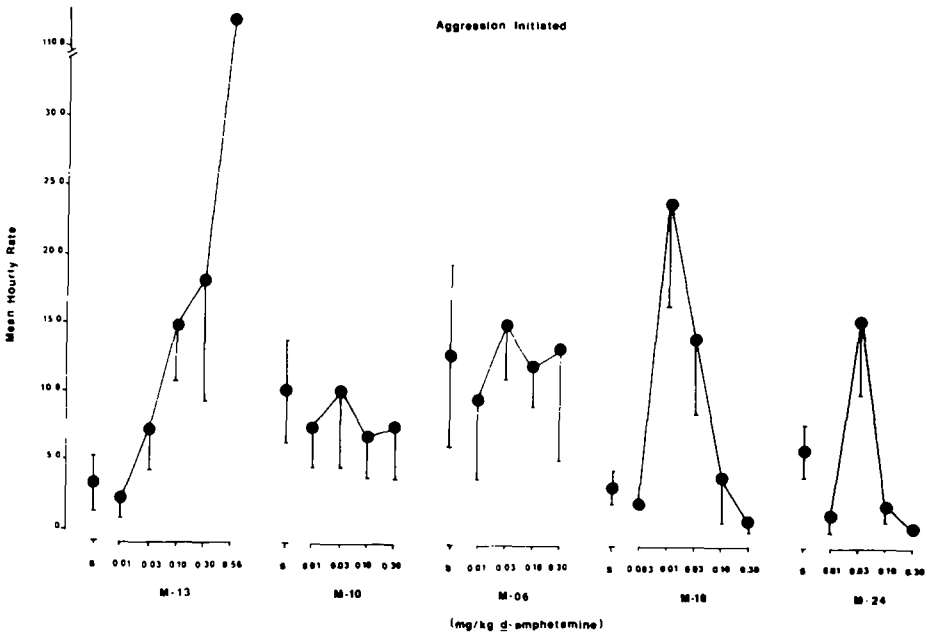

FIG. 2. Effect of *d*-amphetamine on rate of aggressive behavior in five adult male stumptail macaques. Each data point is the mean±SEM based on three administrations (except that the highest dose for M-13 and the lowest dose for M-18 are based on only one administration). Data points to the left of the dose-effect curves were obtained when saline was administered as a control.

ing part of a large, heterogeneous social group. *d*-Amphetamine decreased affiliative behavior to as little as 30% of saline control values, and the effect was monotonic and dose-dependent. In contrast, comparable doses of *d*-amphetamine increased aggression in the same subjects that exhibited marked decreases in affiliative behavior.

The decrease in affiliative behavior observed in the present study is consistent with earlier reports of amphetamine's effects on the behavior of members of social groups. Kjellberg and Randrup [14], Miller and Geiger [18] and Scraggs and Ridley [21] reported dose-dependent decreases in social grooming, a major component of affiliative behavior, following the administration of *d*-amphetamine. Similarly, Schiørring [19] and Schiørring and Hecht [20] studied the effect of amphetamine on mother-infant contact in vervet monkeys *(Cercopithecus aethiops)* and found a reduction in ventro-ventral contact. Grooming and contact were individual affiliative behaviors that also decreased in the present study (Table 2). The uniformity and generality of the reports indicating decreases in affiliative behavior as a consequence of amphetamine administration compel one to regard this effect as characteristic of a number of primate species, especially when constituted as social groups. The mechanism or basis of the differential effect of amphetamine on affiliative behavior is unclear, however.

Given the relatively uniform decrease in the initiation of affiliative behavior following *d*-amphetamine in the present study, the qualitatively dissimilar effect on aggression in the same subjects was striking. The high- and low-ranking subjects exhibited pronounced, dose-related increases in aggressive behavior at doses that either decreased affiliation or had no effect. In the two low-ranking subjects, the dose-effect curves described an inverted U-shaped function characteristic of the effect typically obtained with this drug on operant behavior maintained under certain types of reinforcement schedules [8,16]. Moreover, the range of doses having behavioral effects in the present study was quite similar to the range others have found to have effects on conditioned behavior in various species of nonhuman primates [5, 13, 15]. A similar inverted U-shaped function would presumably have been obtained in monkey M-13, the subject

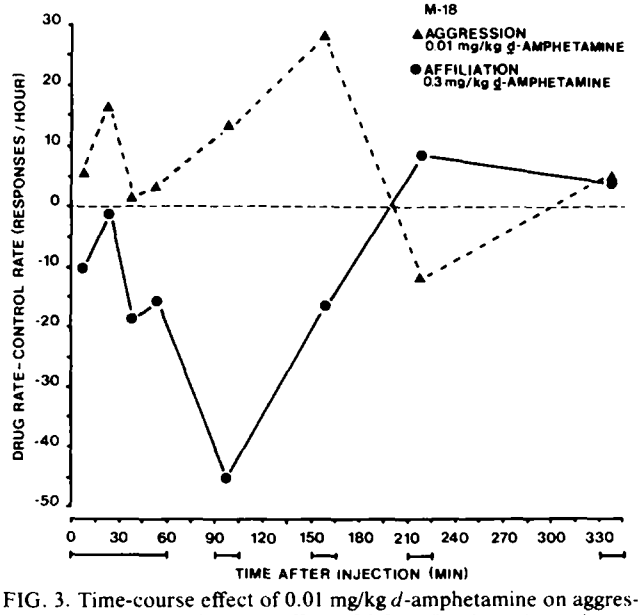

FIG. 3. Time-course effect of 0.01 mg/kg *d*-amphetamine on aggressive behavior (triangles) and effect of 0.3 mg/kg *d*-amphetamine on affiliative behavior (circles) in monkey M-18. Data points are mean differences (drug rate − control rate) based on three administrations of the drug.

exhibiting the greatest increase in rate of aggressive behavior, had higher doses been studied. However, a decision was made not to administer higher doses because (a) this subject increased aggression so markedly at 0.56 mg/kg and (b) the safety of that monkey and other members of the group that might become objects of his aggression was deemed to be of greater importance.

In addition to the qualitatively different effects of *d*-amphetamine on affiliative and aggressive behaviors, the present study provides additional evidence that the effects of this drug are a function of processes evolving out of group dynamics, e.g., interactions between one animal and others occupying the same environment or the dominance hierarchy characteristic of a group. *d*-Amphetamine produced marked increases in rate of aggression in the high- and low-ranking subjects but did not cause similar changes in the behavior of mid-ranking subjects. Moreover, the dose-effect curve for the highest-ranking member of the group was shifted to the right more than one log unit relative to the other subjects that showed increased responding. These differences in effects suggest that the hierarchical or dominance position of an individual subject in a group may serve as a determinant of the extent to which a drug such as *d*-amphetamine can alter ongoing behavior characteristic of that individual. This hypothesis is supported by other reports that various psychoactive drugs can act selectively to alter the behavior of individual members of a group [7, 10, 17].

Analysis of the time course of the effects of *d*-amphetamine revealed that the duration of action of the drug on naturally-occurring behavior was comparable to the duration on conditioned or learned behavior. Previously, Gonzalez and Goldberg [9] described the time course of the effects of two CNS stimulants on schedule-controlled behavior in the squirrel monkey, and their functions for *d*-amphetamine paralleled those reported here. In both species, common doses of *d*-amphetamine caused deviations from the control or non-drug rate of the behavior that persisted for similar durations. Although not conclusive, these data provide reason to expect that the duration of an effect of *d*-amphetamine on behavior in nonhuman primates will not be different for each type of behavior.

The behavioral effects of *d*-amphetamine and other psychoactive drugs have often been ascribed to rates of responding in the absence of a drug, i.e., to response rates under control conditions [8,13]. That differences in the effects of *d*-amphetamine among the five experimental animals can be attributed to differences in the pre-drug or control rates does not seem tenable in the present study, however. Monkeys M-13 and M-06 had similar rates of affiliative behavior under non-drug conditions (20 and 23 per hour, respectively), yet *d*-amphetamine had qualitatively different effects in the two subjects. The former monkey showed an orderly, monotonic decrease in rate as dose increased and the latter showed no decrease. Moreover, monkeys M-13 and M-18 had identical rates of aggression under non-drug conditions (3 per hour), yet *d*-amphetamine produced much larger increases in rate of aggressive behavior in M-13 than in M-18, and the doses producing the maximum increases in the two monkeys differed by a factor of 56. Differences in the effects of *d*-amphetamine on aggressive behavior among the high-, middle- and low-ranking monkeys suggest that the effects were not rate-dependent and that factors associated with dominance positions in the group or dynamics within the group can determine the effects of a psychoactive drug. The extent to which these influences can modulate drug effects is not yet well understood, but studies of the type reported here may provide the information and data needed for a better understanding.

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