

# A Behavioral Analysis of the Effects of Amphetamine on Play and Locomotor Activity in the Post-Weaning Rat

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SUTTON, M E AND L A RASKIN *A behavioral analysis of the effects of amphetamine on play and locomotor activity in the post-weaning rat* PHARMACOL BIOCHEM BEHAV 24(3) 455-461, 1986 — Amphetamine has been shown to canalize or direct the activity of a young rat towards ethologically relevant stimuli. In the five-day-old, amphetamine increases the speed of approach to the nipple of an anesthetized dam, in the 15-day-old, amphetamine increases motor activity and directs it toward an anesthetized adult, however, in the juvenile rat amphetamine reportedly disrupts species-specific behaviors such as huddling and play. The present experiments further assessed the effects of amphetamine in the post-weaning rat by measuring drug-induced behaviors in the presence of an alert and anesthetized companion. In Experiment 1, subjects were videotaped in the presence of an alert non-treated, same-age rat and components of play, a predominant behavior of the post-weaning rat, were recorded. Results confirmed previous reports that low doses of amphetamine (0.5 mg/kg) disrupt play behavior, however, in the present experiment higher doses of amphetamine (1.0 mg/kg) did not disrupt the percentage of time spent in play. Further analysis of drug-induced behavior revealed that the 1.0 mg/kg amphetamine-injected rat engaged in play with the companion, although the drug-treated animal did exhibit marked alterations in the flexibility of its motor patterns. The second experiment confirmed that amphetamine did not disrupt the amount of time a juvenile rat spent with an anesthetized age-mate. In fact, amphetamine-induced activity was directed towards the anesthetized same-age rat. Following amphetamine treatment, all subjects were active nearly 100% of the observation period whether they were tested alone or in the presence of an anesthetized same-age rat. However, subjects that were tested with the anesthetized same-age rat exhibited their activity exclusively around the stimulus. The present experiments suggest that although the flexible motor patterns required for play were disrupted following amphetamine treatment, amphetamine did not disrupt contact between two awake juvenile rats. In the presence of an anesthetized same-age conspecific, amphetamine also potentiated locomotor activity exhibited in the vicinity of that conspecific.

Amphetamine    Post-weaning rat    Play    Locomotion

EVIDENCE suggests that in the immature rat amphetamine-induced activity is focused towards developmentally relevant stimuli [3,15]. When 5-day-old-pups were tested in the presence of an anesthetized dam, amphetamine increased the speed with which pups approached the ventrum of the dam [16]. When 15-day-olds were tested in the presence of an anesthetized adult, amphetamine-induced activity was observed almost exclusively along the ventrum of the adult conspecific [15]. In addition, amphetamine-treated, but not saline-treated 15-day-olds repeatedly followed an anesthetized adult which was pulled along the perimeter of an open field [3]. Consistent with these findings is the report that in the young rat, amphetamine increased the tendency for the animal to seek out and orient towards its home nest area [18].

In contrast to the results reported for immature rats, amphetamine-induced activity in older rats does not appear to be focused towards developmentally relevant stimuli. This notion stems from the finding that when 30-day-olds were injected with amphetamine and tested in the presence of an anesthetized adult, their increased activity was not directed

towards the conspecific. Furthermore, amphetamine-treated 30-day-olds did not follow an anesthetized adult rat which was pulled along the perimeter of an open field [3]. This pattern of results suggested that amphetamine focuses or canalizes arousal towards developmentally relevant stimuli early in life but as maturation proceeds this tendency gradually disappears [3]. Another interpretation of this pattern of results can also be considered. It is possible that amphetamine-induced activity is directed towards salient stimuli throughout ontogeny and that an anesthetized adult rat is not an appropriate stimulus for an older juvenile rat. In contrast to younger rats, the 30-35-day-old rat spends little time in the nest except for sleep time [2] and is involved in social interactions with its age-mates, particularly in play behavior. In fact, a multivariate analysis of the rats' behavior has revealed that play behavior peaks between 25 and 35 days, declining sharply thereafter [6]. Given that play is a vital part of the normal social development of the rat [2, 11, 12, 13] and that the incidence of sibling interaction is increased in the rat around the time of weaning, a same-age companion might constitute an age-appropriate stimulus for

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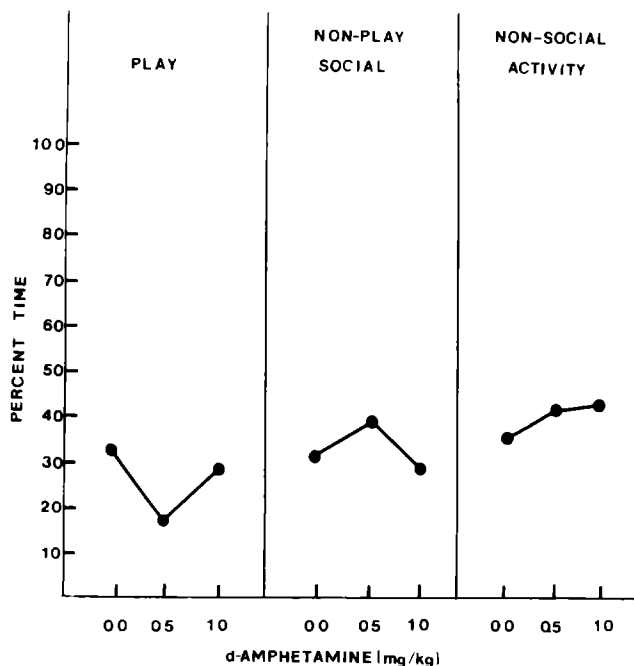


Fig 1 Percentage of time juvenile animals spent in play, non-play, social behavior and non-social activity plotted as a function of drug dose

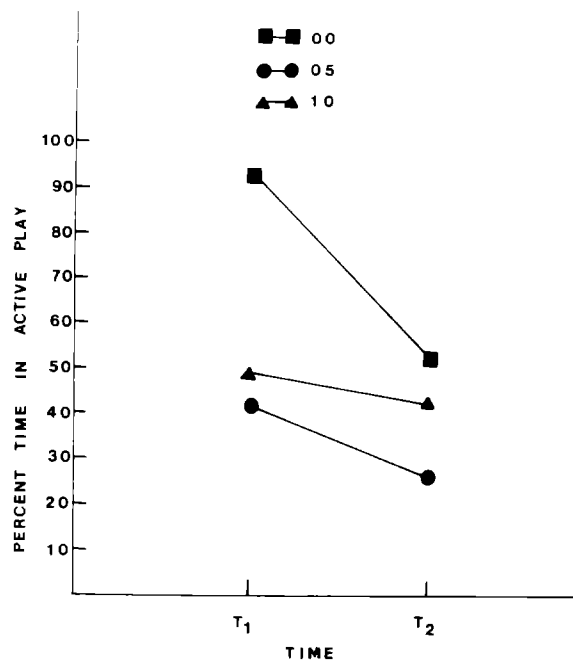


FIG 2 Percentage of time spent in active rough-and-tumble play plotted as a function of dose of amphetamine and time period

the post-weaning rat. Consequently, in the first experiment of this report, animals were given amphetamine and tested in the presence of an alert same-age companion.

If amphetamine acts to focus or direct activity in the post-weaning rat it could be predicted that amphetamine would potentiate play behavior at this age. Although not directly addressing this issue, previous experiments have shed light on the effects of amphetamine on play behavior. Beatty *et al* [1] administered d-amphetamine to both members of a pair of rats between 26–46 days of age and found that amphetamine produced a dose-dependent decrease in play along with a dose-dependent increase in social investigation. What was not determined in this report is how play behavior would be influenced if only one member of the dyad was treated with amphetamine. In addition, the observations lasted only ten minutes and therefore represent a small sample of behavior. Similarly, Humphreys and Eison [9] used a T-maze to examine the reinforcing properties of play for juvenile rats and also found that amphetamine reduced play behavior and increased social behavior. In their experiment, animals were also observed during the short observation session which lasted only one minute. Therefore, the first experiment of the present report investigated the effects of amphetamine on play behavior in post-weaning 32–35-day-old rats by administering amphetamine to one member of a dyad and recording behavior during an hour observation period.

The second experiment sought to determine if amphetamine-induced activity would be directed towards an anesthetized conspecific if that conspecific was an age-mate, rather than an adult. Thus, animals were injected with d-amphetamine and their activity was measured while in and out of contact with an anesthetized age-mate.

EXPERIMENT 1

The purpose of this experiment was to examine the effects of d-amphetamine on play behavior in 32–35-day-old rats. A subject rat, who had been given saline or amphetamine, and a “companion” rat were videotaped together for one hour. The videotapes were then scored in order to assess whether amphetamine caused any changes in the amount of time the subjects spent in three broad categories of behavior: play behavior, non-play social behavior, and non-social activity.

Subjects

Subjects were thirty-six male and twelve female 32–35-day-old Sprague-Dawley rats bred and raised in the Amherst College colony. Twenty-four of the males were used as play companions. At three days after birth, all litters were culled to eight pups and remained housed with the mother in standard maternity cages until they reached 30 days of age. At this time all animals were weaned and housed singly in 25×19×21 cm hanging wire cages. Animals were housed in isolation, given that short periods of social deprivation produce a “play rebound” which increases the percentage of time young rats engage in this complex behavior [13]. Except during testing, animals had free access to food and water. The colony was maintained on a reverse dark-light cycle (12 hr dark/12 hr light), with all testing taking place from 1 p.m. to 5 p.m., during the second half of the dark phase.

Apparatus

All behaviors were observed in a 62×32×32 cm glass

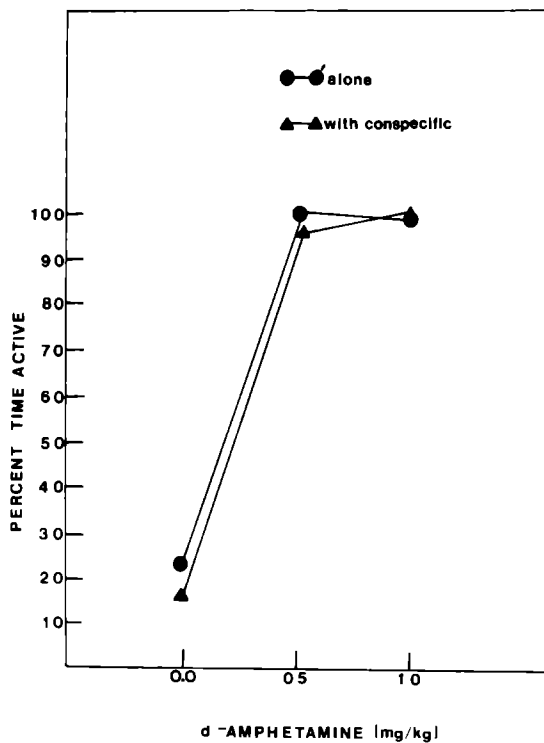


FIG 3 Percentage of time juvenile animals spent active following amphetamine treatment while alone or in the presence of an anesthetized same-age conspecific

aquarium, with wood shavings covering the floor. The testing room was illuminated by two 50 watt red light bulbs

#### Procedure

Subjects were tested at 32–35 days, the age range during which play behavior peaks in the rat [6]. A split litter design was employed so that no more than two animals from each litter were placed in each experimental group. On test days, subjects were removed from their cages, weighed, and injected intraperitoneally (IP) with either 0.5 or 1.0 mg/kg d-amphetamine sulfate dissolved in 0.9% saline or the saline vehicle. Subjects were then marked on the back with non-toxic black magic marker and placed in the testing apparatus with a same-age companion who was also naive to the task. The pair was left undisturbed for 30 minutes, after which a videotape recorder was turned on for the 60 minute testing period.

#### Data Analysis

All videotapes were scored by an experimenter blind to the subject's drug treatment. For three 20-minute sessions, the experimenter recorded the percentage of time the subject spent in three broad categories of behavior: play behavior, non-play social behavior, and non-social activity. Play behavior was defined to include the following behaviors: rough-and-tumble play, a spirited wrestling behavior involving both animals, pounce on, subject lands with forelimbs on companions back, boxing, both animals rear on back legs and contact each other with forelimbs, pin, subject flips companion onto its back and holds it there with forelimbs, pinned, companion does the same thing to subject, chase, subject runs closely behind the companion, chased, compan-

ion runs closely behind subject. Non-play social behavior was defined to include all behaviors, other than play, that the awake subject exhibited while in contact with the companion. These behaviors included: groom companion, groomed by companion, sniff companion, sniffed by companion, huddle with companion (usually in conjunction with other behaviors, such as dig, mount, follow, followed, and climb over). The third category, non-social activity, consisted of behaviors exhibited by the subject while alone and awake. These behaviors included: walking, sniffing (head pointed towards the ground or in the air), digging, chewing shavings, rearing, and running. Once these behavioral categories were established, samples of the tapes were scored by two experimenters who were blind to the animal's condition until inter-rater reliability was at least 90 percent.

The experimenter then scored the videotapes a second time through, again unaware of the subject's drug treatment. This time, the first twenty minute period and the third twenty minute period were scored for the duration of time that the subject spent in active rough-and-tumble play behavior. A time sampling method was used because there was no effect of time found in the first measure of play. This new method was introduced after it was noticed that the animals treated with 1.0 mg/kg d-amphetamine seemed to spend proportionately more of their play time in immobile play positions. Active rough-and-tumble play was defined to include all behaviors in the "wrestling" sequence during which the subject was involved in vigorous movement. All data were analyzed using Analysis of Variance (ANOVA).

#### RESULTS

The results of the first experiment are shown in Fig 1, which depicts the percentage of time that subjects spent in play behavior, non-play social behavior, and non-social activity during the one hour testing period when given 0.0, 0.5, or 1.0 mg/kg d-amphetamine. The three panels represent almost all of the time the animals were being observed. A three-way ANOVA for each behavioral category (sex of companion  $\times$  time period  $\times$  dose) did not show any significant effects for time period or sex of companion, so the results were collapsed across all three time periods as well as for both sexes of the companions. One-way ANOVAs were then performed for each category of behavior. As can be seen in the first panel of Fig 1, the percentage of time subjects spent in play decreased at 0.5 mg/kg and, surprisingly, returned to the saline level at 1.0 mg/kg. A one-way ANOVA confirmed a significant effect of dose,  $F(2,21)=7.49$ ,  $p<0.01$ , which reflected the decrease in percent time spent in play at 0.5 mg/kg.

Panel 2 depicts the percentage of time subjects spent in non-play social behavior, defined as all behaviors other than play that the awake subject exhibited while near or in contact with the companion during the one-hour testing period. The mean percentages of time spent in non-play social behavior for the three doses created a curve which approximates an inverted V-shape, a mirror reflection of the results for play. The amount of non-play social behavior increased from 0.0 to 0.5 mg/kg and decreased back to saline levels at 1.0 mg/kg. A one-way ANOVA confirmed a significant effect of dose,  $F(2,21)=6.037$ ,  $p<0.01$ , for non-play social behavior. The percentage of time subjects spent in non-social activity, which was defined as any active behavior exhibited by the subject when alone, is pictured in panel 3 of Fig 1. There was relatively little change in the time spent in this category.

of behavior as amphetamine injection, a finding which was confirmed by a non-significant one-way ANOVA,  $F(2,21)=1.713, p>0.05$

In summary, these results indicated that while subjects exhibited no change across drug dose in the percentage of time they spent active while not in contact with the playmate, at 0.5 mg/kg, d-amphetamine-injected animals spent significantly less time during the hour in play behavior and significantly more time during the hour in non-play social behavior than did subjects at 0.0 or 1.0 mg/kg

Given that the results of this experiment were inconsistent with reports that 1.0 mg/kg amphetamine also disrupts play and facilitates other social behaviors such as grooming, sniffing and huddling with the companion [1], the videotapes were re-scored to more closely analyze the behavioral changes occurring following administration of 1.0 mg/kg amphetamine

The 1.0 mg/kg d-amphetamine group seemed to be engaged in a qualitatively different kind of play than that shown by the saline group in that it appeared to be much less flexible and interactive. In contrast to the saline group's vigorous, rough-and-tumble style of play, the play of the 1.0 mg/kg group appeared to be in slow motion, with these subjects spending more time than the 0.0 mg/kg animals frozen in the positions used for pinning the companion or being pinned by the companion, and not as much time as the saline animals actively maintaining or vying for an offensive position

Thus, the tapes were re-scored to determine if active play, that is, rough-and-tumble play, varied as a function of drug dose. Figure 2 depicts the percentage of time subjects spent in active rough-and-tumble play as a function of time. Both amphetamine groups spent less time in active rough-and-tumble play than the saline group, and all three groups, 0.0, 0.5, and 1.0 mg/kg d-amphetamine, seemed to spend less time in active play during the second time period (T2) than during the first (T1). These observations were confirmed by ANOVA with the effects of dose,  $F(2,21)=9.55, p<0.01$ , and time,  $F(1,21)=8.214, p<0.01$ , being significant. However, the dose by time interaction was not significant. A subsequent ANOVA comparing the two amphetamine groups did not show a significant effect of dose or time or a significant dose by time interaction. The main finding of this experiment was, therefore, that both the 0.5 mg/kg and 1.0 mg/kg groups show similar decreases in the amount of time spent in active play as compared to the saline animals

#### DISCUSSION

The results of this experiment confirmed those previously reported that 0.5 mg/kg decreases play and increases other social behaviors in juvenile rats. The present findings also showed that when play is defined broadly to include rough-and-tumble play (boxing, pinning, chasing), a higher dose of amphetamine did not disrupt play. This finding is largely due to the fact that 1.0 mg/kg amphetamine appeared to disrupt only the most flexible, highly choreographed components of play. When play was defined more specifically as rough-and-tumble wrestling, 1.0 mg/kg amphetamine did significantly disrupt the behavior

The results of these experiments both agree and disagree with those of Beatty *et al.* [1]. While the results for the 0.5 mg/kg animals replicate the findings that d-amphetamine decreases play behavior and increases other amicable behaviors, the results for the 1.0 mg/kg animals do not entirely

support these conclusions. While 1.0 mg/kg amphetamine decreased the amount of time animals spent in rough-and-tumble play behavior, the measures using a more broadly defined play behavior (including pinning, chasing, boxing) remained at saline levels and the time spent in non-play social behavior did not increase. Beatty *et al.* reported that 1.0 mg/kg d-amphetamine almost completely abolished the time subjects spent in play behavior and the number of pins exhibited. The discrepancy between Beatty *et al.*'s results and those of the present experiment could be accounted for by the fact that in the former experiment amphetamine was administered to both animals of each pair. Perhaps amphetamine makes animals less likely to initiate play bouts unless they receive sufficient social stimulation from a normal rat. Humphreys and Eison [9] have shown that amphetamine-treated animals have reduced reinforcing qualities in a T-maze as compared to saline-treated animals, which would support the hypothesis that if both animals were treated with amphetamine, they may not provide each other with a critical level of social stimulation which might be necessary for the initiation of play behavior

Another interesting finding of this experiment is that amphetamine did not increase the time that animals spent locomoting while they were not in contact with companion (non-social activity). According to previous reports, amphetamine directed activity toward developmentally salient environmental cues in the young pup [15,16], but actually decreased the amount of time that 30-day-old rats spend with an anesthetized adult [3]. In this experiment, while amphetamine disrupted the amount of time spent in active rough-and-tumble play, amphetamine did not significantly decrease the amount of time spent with the companion. That is, when play decreased, non-play social interactions increased and the dyad spent the same amount of time together whether the subject had been given the drug or not

However, because the play experiment necessarily involved a moving active companion, these results cannot be used to conclusively show that amphetamine directs activity toward ethologically relevant stimuli in older animals. The behavior of the companion certainly had a large effect on the amount of time the pair spent together or in any one behavioral category. Behavioral measures were taken only of the subject's activity, but the companion could influence the nature of that activity at any time by initiating, maintaining, or terminating contact with the subject. Ideally one hopes to assess how amphetamine influences behavior when animals are tested in a natural environment, however, measuring the subject's behavior as the subject interacts with an alert companion is problematic. Results necessarily reflect variations in the subject's behavior, the companion's behavior, and in the dynamics of the interaction between the two animals

Consequently, Experiment 2 was performed to determine how amphetamine influenced behavior in the presence of a same-age companion, but this time the companion was anesthetized. This experiment was similar to that of Campbell and Randall [3] except that an anesthetized age-mate was used rather than an anesthetized adult

#### EXPERIMENT 2

In this experiment, subjects given either 0.0, 0.5, or 1.0 mg/kg d-amphetamine were tested in one of two environmental conditions in the presence of an anesthetized same-age rat, or alone. The time animals spent in contact with the same-age conspecific as well as in locomotion was recorded

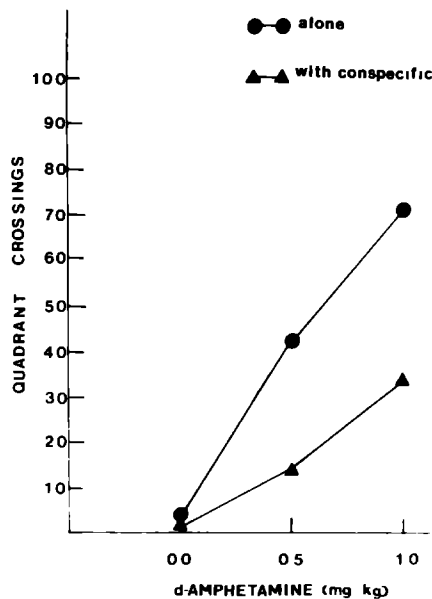


FIG 4 The number of quadrants crossed plotted as a function of drug dose while tested alone or in the presence of an anesthetized age-mate

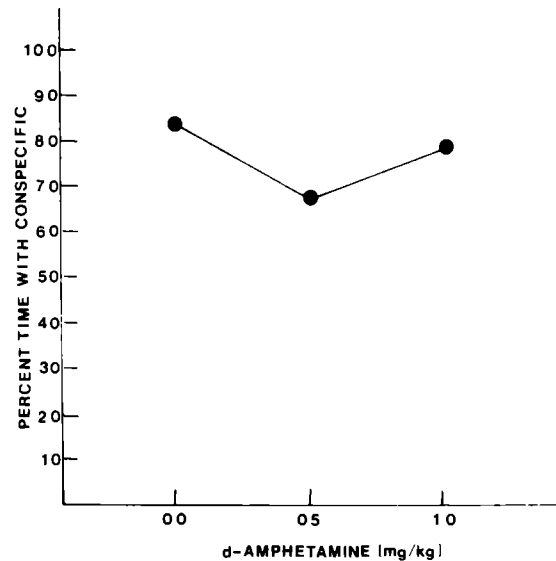


FIG 5 Percentage of time spent in contact with anesthetized age-mate plotted as a function of drug dose

*Subjects and Apparatus*

The subjects were 36 Sprague-Dawley rats born and bred at Gofmoor Farms. Following weaning, they were transferred at approximately 30 days of age to the Amherst College colony and housed singly in 25×19×21 cm hanging wire cages. As in Experiment 1, the colony was maintained on a reverse dark-light cycle, and animals were provided with ad lib food and water. All conditions in the testing room remained the same as in Experiment 1. The test cage was also the same, however, in Experiment 2 the floor of the aquarium was divided in four equal quadrants.

*Procedure*

As in Experiment 1, subjects were tested at 32–35 days, and all testing took place between 1 p.m. and 5 p.m. Subjects were randomly assigned to one of the three drug groups (0.0, 0.5, or 1.0 mg/kg amphetamine) and one of two environmental testing conditions. In the first environmental condition, subjects were observed while alone in the aquarium. In the second environmental condition, subjects were tested in the presence of a same-age rat that had been anesthetized with Nembutal and placed at one end of the aquarium across the length of the short axis of the cage. On the day of testing, subjects were weighed, injected IP with one of the drug solutions, and placed in the aquarium either alone or with the anesthetized rat for a 30 minute habituation period. After the habituation period, an experimenter who was blind to the subject's treatment condition scored the behavior through an observation window. Subjects were observed for thirty minutes and for the isolated subjects the percentage of time active and the total number of quadrants entered were recorded. For the subjects observed in the presence of an anesthetized rat, the amount of time spent in contact with the anesthetized rat was recorded in addition to the aforementioned activity measures.

RESULTS AND DISCUSSION

The results for the second experiment are pictured in Figs 2–4. Figure 2 shows the percentage of time animals in each drug dose group were active during the testing period when tested in two different environments. While the saline group was only active about 15% of the time, both amphetamine groups were active nearly 100% of the time. There was, however, no difference in the amount of time subjects were active as a function of environment, so animals exhibited some type of activity for the same percentage of the test session whether or not they were in the presence of the anesthetized rat. Saline animals appeared to sleep for a great deal of the time in both environments yet amphetamine-treated rats remained active for nearly all of the test period in both environments. A two-way ANOVA confirmed a significant effect of dose,  $F(2,30)=156.2, p<0.01$ , but no effect of environment and no significant environment by drug dose interaction for the amount of time subjects spent active.

Figure 3 shows the number of times that animals crossed over into a different quadrant plotted as a function of drug dose when animals were tested either alone or with the anesthetized conspecific. Animals in both environments showed a dose-dependent increase in the number of quadrants crossed, however, animals tested with the conspecific clearly showed less quadrant crossings than those tested alone. A two-way ANOVA verified these observations, with a significant effect of environment,  $F(1,30)=6.98, p<0.05$ , as well as dose,  $F(2,30)=12.65, p<0.01$ , but no environment by dose interaction.

Thus, in the presence of an anesthetized conspecific, amphetamine-treated animals showed high levels of activity (active 100% of the time) but actually crossed into fewer quadrants than those amphetamine-treated animals that were tested alone. In fact, amphetamine-injected animals which were tested in the presence of an anesthetized same-age rat spent most of their time active in the presence of that

stimulus. This is depicted in Fig 4, which shows that following amphetamine administration there was no significant disruption in the amount of time animals spent in contact with the anesthetized conspecific,  $F(2,15)=0.386$ ,  $p>0.05$ . Thus, if the results from Figs 2, 3 and 4 are taken together it appears that following amphetamine treatment with either 0.5 or 1.0 mg/kg, juvenile animals are active throughout the observation period, regardless of whether they are tested alone or in the presence of a same-age companion. Amphetamine does not disrupt the amount of time animals spend in contact with an anesthetized same-age conspecific. In the presence of an anesthetized age-mate the amphetamine-treated animal crosses fewer quadrant lines than when alone, and exhibits its increased activity within the area quadrants containing the conspecific.

#### GENERAL DISCUSSION

The results of the first experiment of this report confirmed others which show that amphetamine disrupts play and increases social investigation in the juvenile rat [1]. A similar finding has also been reported following the administration of caffeine, another type of psychomotor stimulant [8]. The fact that the 1.0 mg/kg amphetamine group did not show a decrease in overall play behavior in the present experiment is not really inconsistent with other reports. Although the amount of time amphetamine-treated animals spent with the playmate did not decrease following the 1.0 mg/kg dosage, there was a dramatic change in the nature of their play bouts. Following 1.0 mg/kg, amphetamine-treated animals showed behaviors which were similar to stereotypic movements, in that they would obtain a position and persevere in that position during such behaviors as pinning or being pinned by the playmate. Thus, following 1.0 mg/kg amphetamine, animals showed a significant decrease in active rough-tumble play, suggesting that although the quantity of their interaction did not change, the components of their play bouts did.

The findings of Experiment 1 also showed that, although amphetamine disrupted certain behaviors between the dyad, the amount of time the two animals spent in contact did not seem to change as a function of drug treatment. Amphetamine-treated animals were either involved in social investigation, or in a less flexible, less mobile play, however, they remained together and did not show a drug-induced increase in non-directed activity. This finding suggests that amphetamine alters qualitatively but does not abolish social behaviors in juvenile rats. An amphetamine-induced disruption of conspecific contact was previously observed when amphetamine-treated 30-day-olds were tested in the presence of an anesthetized adult [3].

The finding that amphetamine did not disrupt the amount of time animals spent together in Experiment 1 could have been because the target stimulus was an awake same-age companion rather than an anesthetized adult rat. Given that the companion was awake and its behavior necessarily influ-

enced that of the amphetamine-treated subject. Experiment 2 was run to determine the effects of the presence of an anesthetized same-age rat on the behavior of an amphetamine-treated juvenile rat.

Taken together, the results of Experiment 2 suggested that when post-weaning rats were tested in the presence of an anesthetized age-mate, amphetamine-induced activity was directed towards the conspecific. In these animals the percentage of time spent active increased, the percentage of time spent with the age-mate did not decrease and the number of quadrant crossings exhibited was significantly less than that of amphetamine-treated animals tested alone. This reflects the finding that amphetamine-treated animals showed an increase in activity which was not expressed in forward locomotion, but rather was exhibited around or on the conspecific.

The results of both Experiments 1 and 2 suggest that low doses of amphetamine alter, but do not decrease, the amount of social behavior exhibited by juvenile rats. Certain social behaviors (i.e., play) are disrupted by low doses of amphetamine, while other social behaviors (i.e., social investigation) are even potentiated. In addition, it appears that locomotor activity exhibited by an amphetamine-treated juvenile rat is directed towards an anesthetized conspecific if that conspecific is of the same age as the subject. This finding refutes the notion that amphetamine has a differential or paradoxical effect on the behavior of young and older juvenile animals, as was previously suggested by Campbell and Randall [3]. It rather suggests that amphetamine might potentiate certain species specific behaviors in the rat, such as social investigation or activity which is directed towards an age-appropriate stimulus, such as a same-age conspecific.

While some studies involving adult animals have shown that amphetamine disrupts species specific social behaviors, such as affiliative and agonistic behavior in monkeys [11], this disruption may depend primarily on dosage and environmental variables, or on the particular species and behavior being examined. For example, Schiorring and Randrup [17] have shown that although low doses of amphetamine (1 mg/kg) did not change social interaction in adult rats, higher doses of amphetamine (3 mg/kg) significantly disrupted huddling behavior. Others have shown [7] that low doses of amphetamine actually potentiated social behavior in adult rats. The findings of these experiments suggest that throughout development in the rat, low doses of amphetamine potentiate specific types of activity toward ethologically relevant stimuli. That there are similar behavioral effects of low doses of amphetamine in adult, juvenile, and immature rats is consistent with the clinical findings of Rapoport and her colleagues [14]. They have shown that amphetamine produces similar effects in increasing vigilance and improving performance in normal adult men, as well as in normal and hyperactive children. The present paper further questions the previously suggested "paradoxical" effect that amphetamine has in rats at different developmental stages [3].

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