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# Psychomotor Stimulants, Social Deprivation and Play in Juvenile Rats[1]

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BEATTY, W W , A M DODGE, L J DODGE, K WHITE AND J PANKSEPP *Psychomotor stimulants, social deprivation and play in juvenile rats* PHARMAC BIOCHEM BEHAV 16(3) 417–422, 1982 —Treatment with d-amphetamine (0 125–1 mg/kg) or methylphenidate (0 5–4 mg/kg) caused dose-dependent decreases in play fighting in juvenile rats which were independent of sex and strain Although brief social isolation profoundly increased play fighting, qualitatively similar drug effects on play were observed in socially housed and isolated animals By contrast, at the highest doses tested both amphetamine and methylphenidate increased social investigation, but only if the rats were socially isolated Stimulation of catecholamine systems is evidently incompatible with the expression of playful behavior

Play Social behavior Amphetamine Methylphenidate Catecholamines Social isolation

DURING the juvenile period, rats, as well as the young of several other mammalian species engage in behaviors that are variously termed play fighting or rough and tumble play Although the play fighting of juveniles often resembles the intraspecific aggressive behavior of adults in terms of the morphology of the responses, juvenile play fighting differs from aggression in adults in a number of important respects [1] For example, in the play fighting of rats the threatening vocalizations (e g , tooth chattering) of adult aggression are absent, biting responses are inhibited so that wounds are extremely rare and dominance–submission relationships are considerably less stable than in adult social encounters In play fighting the roles of "chaser" and "chasee", "on-top" and "on-bottom" are frequently reversed

Ontogenetic studies in rats [13,18] indicate that play fighting appears just before weaning and reaches maximum frequency between 25–45 days of age Thereafter, play fighting declines as adult sexual and agonistic behaviors emerge During the prepuberal period, brief periods of social isolation (social deprivation) cause profound increases in play fighting [19] During this stage of development young rats will learn a maze for the opportunity to play with another animal, treatments that reduce the playfulness of the target animal attenuate its reward value [10]

Thus, play fighting seems to possess several of the characteristics of other motivated behaviors In an attempt to understand the neurochemical mechanisms that control play fighting we began a series of psychopharmacological studies Preliminary studies [17] indicated that 1 mg/kg treatment with d-amphetamine depressed pinning, chasing and other measures of play fighting The present experiments were intended to examine the dose-dependency of this effect and to compare the influence of amphetamine and the pharmacologicaly similar agent, methylphenidate

## EXPERIMENT 1

### METHOD

*Animals*

Subjects were male albino rats obtained from the Holtzman Co , Madison, WI and shipped to the NDSU laboratory at 21 days of age Different groups of rats were used in the amphetamine (N=23) and methylphenidate (N=22) segments of the study which were performed 8 months apart Except during isolation treatments the rats were housed in pairs in standard laboratory cages with free access to food and water in an air conditioned animal room that was illuminated from 0700–1900 During the social isolation condition they were caged singly for 24 hours prior to testing

*Procedure*

Two to three days before testing the rats were habituated to the apparatus, a 51×32×47 cm high box made of plywood

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and clear plastic (see [19] for details) All testing occurred within two hours of the start of the dark portion of the LD cycle Social behavior was studied when the rats were 26–42 days old Pairs of animals were tested for 10 min-long sessions on alternate days under socially housed or isolated conditions at one of four drug conditions For each test pairs were composed of partners that were strangers (i e , animals that had no social contact with one another after arrival in the laboratory) This was accomplished by repairing the rats before each test Both members of a pair received the same drug and social housing treatment Animals in the amphetamine study received 0, 0 25, 0 5 or 1 0 mg/kg d-amphetamine sulfate while rats in the methylphenidate study received 0, 0 5, 2 0 or 4 0 mg/kg methylphenidate HCl Both drugs were dissolved in physiological saline and administered IP 20 min before the start of testing Doses chosen were intended to provide a comparable range for each agent, drug substitution studies [9] indicate that in rats d-amphetamine is 2–4 times as potent as methylphenidate on a weight basis The order of social housing and drug treatments was counterbalanced with 48 hr between tests for all animals, altogether 11 pairs were tested in each combination of drug and social housing conditions in both the amphetamine and methylphenidate phases of the study

Social behavior was assessed by two raters One rater counted the frequency of rearing responses made by the pair (either rat raises its forepaws at least 1 cm off the floor anywhere in the test chamber) and the frequency of pins (one rat rolls the other onto its dorsal surface and stands over it) The other rater scored the duration of time spent by each pair in play fighting, chasing or social investigation from videotape recordings of the sessions Both raters were unaware of the treatment conditions and their blindness was assessed and confirmed by the method of Beatty [2] As a detailed description of the scoring method has been published [19] only a brief description will be provided here *Social investigation* included social sniffing and grooming, which was primarily directed at the anogenital area *Following* consisted of active pursuit (chasing) of one rat by the other and was usually temporally associated with play fighting Sometimes one rat would begin to sniff the anogenital area of another and continue to engage in this behavior as the other animal moved away Such interactions were scored as social investigation *Play fighting* was a composite of several behaviors including tail-pulling, boxing, wrestling, pinning and aggressive grooming Aggressive grooming could be distinguished from social grooming in that it was more intense, almost always directed at the head and neck, and inevitably provoked struggling or squealing by the recipient

Since repeated administration of amphetamine and related agents may lead to the gradual development of sensitization or tolerance (see [20]), we initially examined the data for evidence of order effects As no reliable order effects were detected, the data were collapsed across this variable Because the order of drug exposure differed for each rat as well as for the various pairs, an analysis of tolerance and sensitization is beyond the scope of the present data But since treatments were counterbalanced, such influences, if they exist, should have increased variability without affecting differences among treatment means

## RESULTS

The data were initially subjected to completely factorial analyses of variance (2 levels of Housing Condition × 4 Drug Doses) Separate analyses were conducted for the amphetamine and methylphenidate segments of the experiment As seen in Figs 1–4 social isolation profoundly affected most measures of social behavior in both the amphetamine and methylphenidate phases of the study, confirming earlier findings Social isolation increased the frequency of pinning and the duration of time spent in play fighting and chasing, $F(1,80) \geq 17\ 99$, all $p < 0\ 001$ By contrast, isolation reduced the number of rearing responses (Fig 5), $F(1,80) \geq 5\ 58$, $p < 0\ 05$) but the main effect of Housing Condition was not significant on the social investigation measure

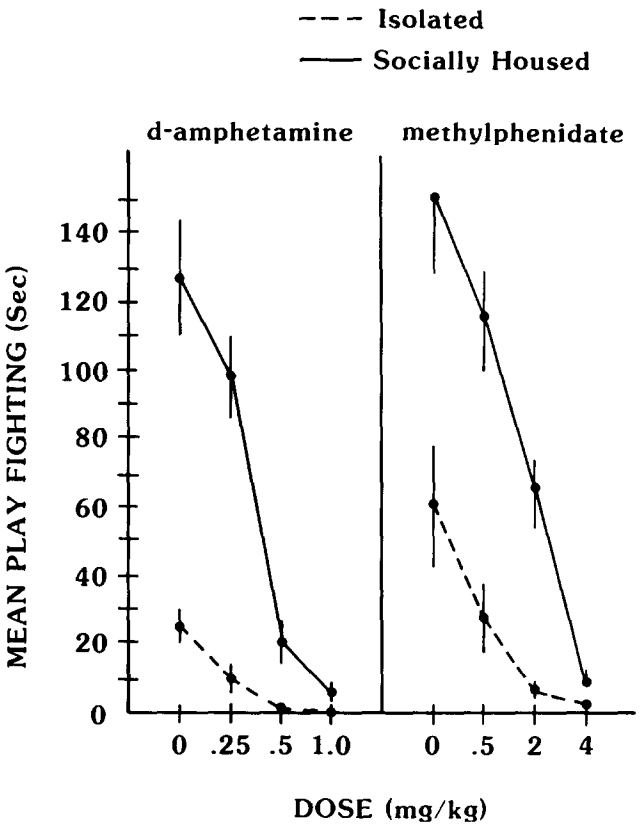


FIG 1 Mean duration of play fighting per pair of rats tested at varying amphetamine and methylphenidate doses (±SEM)

Because of the powerful influence of social isolation and the presence of Drug Dose × Housing Condition interactions on many measures, drug effects were analyzed separately for the social and isolated housing conditions Both amphetamine and methylphenidate reduced play fighting in a dose-dependent manner The effects were qualitatively similar in isolated and socially housed groups, but the magnitude of the drug effects was somewhat greater if the rats were socially isolated Similar drug effects were observed on the time spent play fighting (Fig 1, $F(3,40) \geq 7\ 06$, $p < 0\ 001$ and the number of pins (Fig 2, $F(3,40) \geq 3\ 16$, $p < 0\ 05$) Subsequent analyses with $t$-tests showed that amphetamine at doses of 0 5 mg/kg or greater or methylphenidate at doses of 2 mg/kg or higher reliably depressed play fighting and pinning (relative to the saline control condition) under both housing conditions At the lowest doses (0 25 mg/kg amphetamine, 0 5 mg/kg methylphenidate) qualitatively similar trends were observed on these measures The lowest dose of amphetamine reliably depressed pinning under both housing

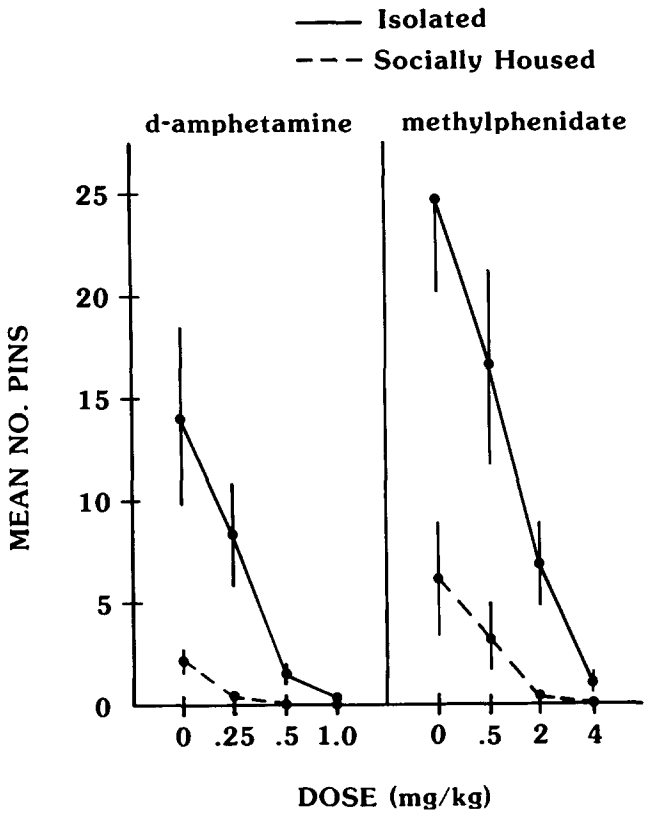


FIG 2 Mean frequency of pinning responses per pair of rats tested at varying amphetamine and methylphenidate doses (±SEM)

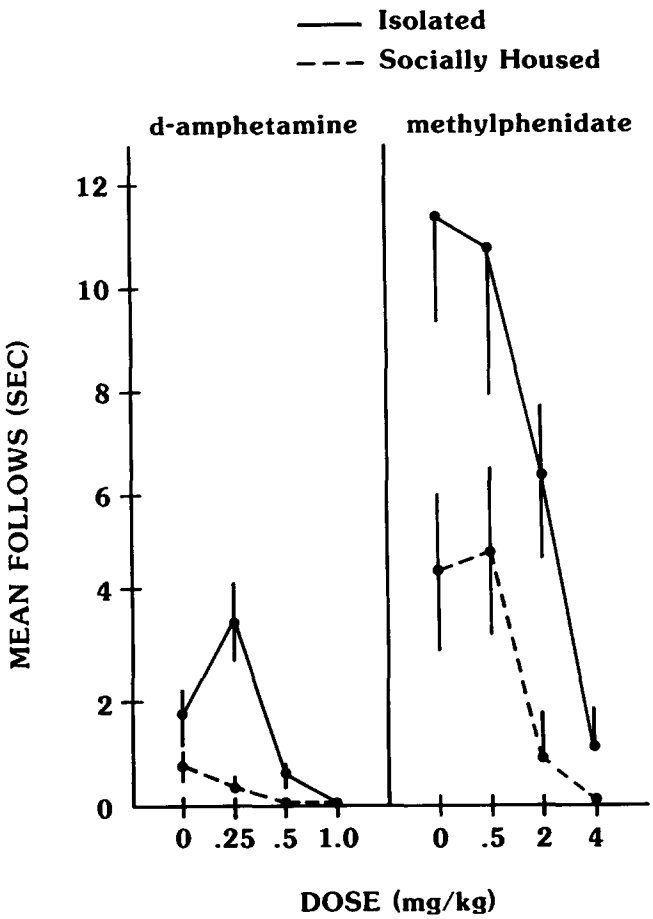


FIG 3 Mean duration of following per pair of rats tested at varying amphetamine and methylphenidate doses (±SEM)

conditions and playfighting when the rats were socially housed The lowest dose of methylphenidate also significantly depressed playfighting when the animals were housed socially, but other comparisons did not reach statistical significance

Stimulant administration generally depressed the time spent following as well (Fig 3, $F(3,40) \geq 4\ 09$, $p<0\ 02$) Subsequent $t$-tests indicated that treatment with 0 5 or 1 0 mg/kg amphetamine or 2 or 4 mg/kg methylphenidate reliably depressed following regardless of whether the rats were housed socially or in isolation At the lowest dose of amphetamine, following was reliably enhanced, but only if the rats were socially isolated Subsequent work (See Experiment 2) suggests that this effect is not reproducible Otherwise the lowest doses of amphetamine and methylphenidate had no reliable effects on following

By contrast, stimulant administration increased the time spent in social investigation (Fig 4) but only if the rats had been socially isolated, $F(3,40) \geq 5\ 18$, $p<0\ 01$ This effect was reliable only at the 1 mg/kg dose of amphetamine and at the 2 and 4 mg/kg doses of methylphenidate When the animals were housed socially no consistent drug effects were evident Rearing (Fig 5) was not reliably affected by either drug ($F<1\ 65$)

## EXPERIMENT 2

The second experiment was a systematic replication of the first with the inclusion of a lower dose of amphetamine as well as an analysis of whether amphetamine modified satiation of play behavior during an extended test session Since play behaviors decline markedly during extended observation periods, it was deemed important to determine the effects of amphetamine at a time when it is declining in controls It is conceivable that amphetamine, through its effects on motor arousal, could sustain social play at such points in time Since they appear to be the simplest and most objective indicator variables for the incidence of play [19], only pinning and following behaviors were monitored in this experiment

### METHOD

*Animals*

Twenty-four Long-Evans hooded rats of both sexes from four litters, bred and born at the BGSU laboratory were used as subjects Animals were socially housed in family groups until 30 days of age, at which time all animals were rehoused individually in 23×10×13 cm wire cages Food and water were freely available

*Apparatus*

Play testing occurred in a 31×31×32 cm Lucite test cage situated in a soundproof outer chamber with a 10 × 10 cm

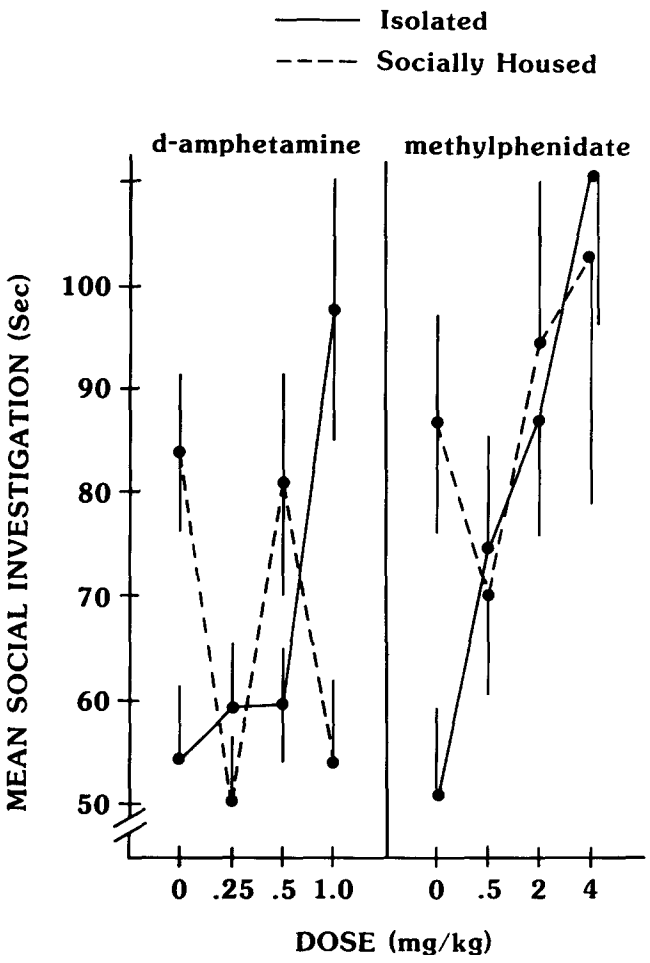


FIG 4 Mean duration of social investigation per pair of rats tested at varying amphetamine and methylphenidate doses (±SEM)

observation window The floor of the chamber was covered with wood-chip bedding, and the only illumination was from a 25 W red light bulb mounted adjacent to the test cage

*Procedure*

Isosexual test pairs were formed at random and remained constant throughout the experiment Otherwise testing conditions were similar to the first experiment except that a 30 minute test period was used, and behavior was monitored for three 5 minute periods (0–5, 10–15 and 20–25 minutes) The measures recorded were frequency of pins and follows Prior to the first series of amphetamine tests, animals were permitted to play for half an hour in the test chambers for four successive test days During the first amphetamine experiment, animals were tested in counterbalanced manner 30 minutes following subcutaneous injection of saline carrier (1 ml/kg), 1 0 mg/kg and 0 5 mg/kg of d-amphetamine Both members of the pair received the same drug treatment One day was allowed between successive test days Thus testing in this study occurred when animals were 36, 38 and 40 days of age

Following this series, animals were retested in identical fashion following s c injections of saline carrier, 0 25 and

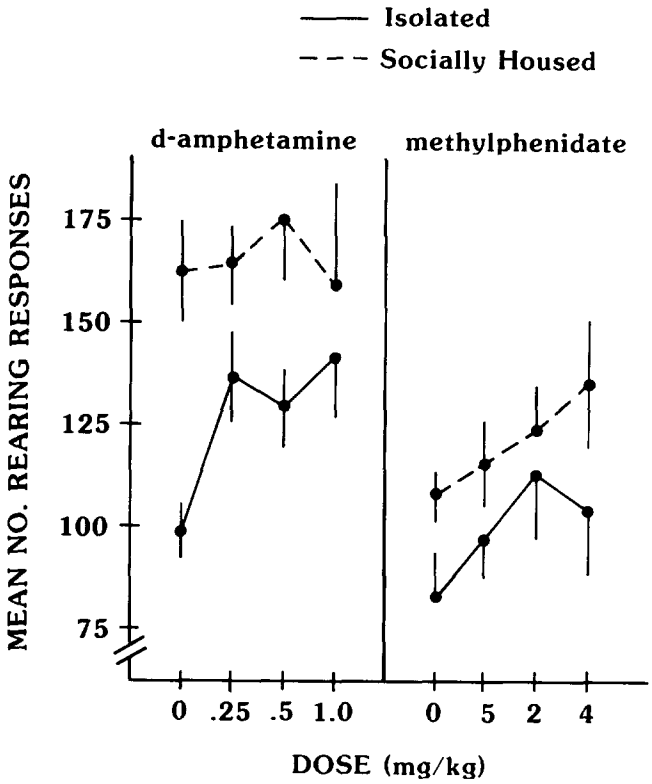


FIG 5 Mean frequency of rearing responses per pair of rats tested at varying amphetamine and methylphenidate doses (±SEM)

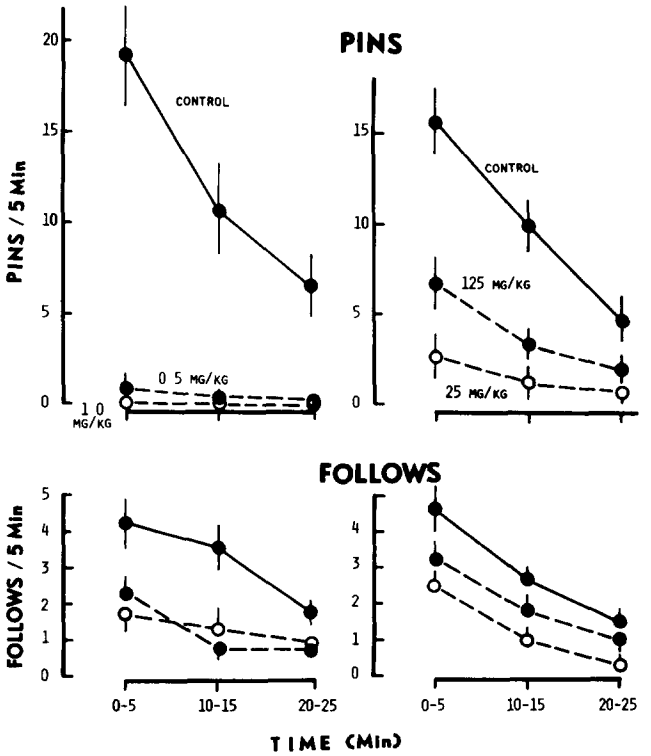


FIG 6 Mean frequency of pinning and following responses per pair of rats tested at different amphetamine doses and different 5 minute periods within the test sessions of Experiment 2 (±SEM)

0 125 mg/kg of d-amphetamine Animals were 42, 44 and 46 days of age during these tests The rater was blind to the treatment conditions

RESULTS

The ability of amphetamine to reduce play was apparent at all drug doses and at all test intervals employed Pinning and following declined systematically during the course of each test session, $F(2,22) \geq 12\ 75$, $p<0\ 001$ for all four comparisons, and amphetamine systematically reduced both play and following in all experiments, $F(2,22) \geq 8\ 26$, $p<0\ 002$ Because of the rapid decline in number of pins in control animals during the course of a test session, the interaction between drug and time was reliable in both experiments with pinning as the dependent measure, $F(4,44) \geq 7\ 51$, $p<0\ 001$ With following, this interaction was marginally significant in the first series of tests with higher doses, $F(4,44)=2,59$, $p<0\ 05$, but not the second There were no sex differences on either measure

## DISCUSSION

Play fighting is remarkably sensitive to the effects of amphetamine and methylphenidate Doses of these agents which were too low to stimulate rearing responses (Experiment 1) and are ordinarily insufficient to enhance locomotor activity in rats of this age [3,4] caused profound and dose-dependent suppression of active play Variables such as the sex and strain of the animals, whether they were housed socially or in isolation immediately prior to testing and the degree of familiarity of the play partners with one another seem relatively unimportant as qualitatively similar drug effects on play were observed in all conditions Likewise, frequency and duration measures yielded quite similar results These and other variables may affect the magnitude but not the nature of the behavioral effects

The present data suggest that activating central or peripheral catecholamine systems is incompatible with the expression of the most vigorous forms of play Whether this is due to a reduced need for social interaction, inhibition of neural mechanisms controlling specific play sequences or the activation of competing responses is not at present clear As described above enhanced locomotor activity and rearing are not likely explanations of the drug-induced reduction in play However, both amphetamine and methylphenidate increased social investigation in the isolated pairs This suggests that these stimulants do not simply reduce the need for social interaction, at least for the socially isolated animals, rather these agents seem to redirect social responding, facilitating social sniffing and grooming and at the same time inhibiting chasing, wrestling and other components of play fighting Recent work by Humphreys and Einon [10] appears to be in excellent agreement with our results In a study that was directly concerned with the reinforcing value of play they observed the interactions of an undrugged juvenile rat with either an amphetamine-treated animal or a saline control The amphetamine-treated rats played much less than controls, but spent more time in other social behaviors such as sniffing and crawling over and under Rats given the 2 mg/kg amphetamine dose did not initiate play nor did they respond to the play invitations of other rats

Since there is a large literature demonstrating that the dopamine-stimulating agents l-dopa and apomorphine potentiate intraspecies aggression in adult rodents [11, 12, 15], it may seem paradoxical that amphetamine and methylphenidate depress play fighting in juvenile rats Two considerations make this apparent discontinuity less surprising than it first appears First, the effects of amphetamine on intraspecies aggression in adult rats and mice are quite complex, aggression can be facilitated or depressed depending on dosage, duration of treatment, as well as a variety of features of the environment [5, 6, 7, 14, 15, 21] In general low doses of amphetamine tend to enhance attack and threat while higher doses suppress these behaviors, but the drug effects are often dependent on the dominance status of the subject [14] and the duration and temporal pattern of treatment [16,20] Second, as discussed in the introduction, play fighting is not simply aggressive behavior performed by young animals In particular, highly stable dominance relationships are not characteristic of play fighting Since amphetamine most often potentiates attacks by dominant animals and facilitates withdrawal or defensive responses by subordinates [7, 8, 14], it is probably not surprising that the drug's effect on play fighting is not identical to its influence on adult aggressive behavior

## REFERENCES


1 Aldis, O *Play Fighting* New York Academic Press, 1975
2 Beatty, W W How blind is blind? A simple procedure for estimating observer naivete *Psychol Bull* **78** 70–71, 1972
3 Campbell, B A , L D Lytle and H C Fibiger Ontogeny of adrenergic arousal and cholinergic inhibitory mechanisms in the rat *Science* **166** 635–637, 1969
4 Campbell, B A and P J Randall Paradoxical effects of amphetamine on preweanling and postweanling rats *Science* **195** 888–891, 1977
5 Eison, M S , W J Wilson and G Ellison A refillable system for continuous amphetamine administration effects upon social behavior in rat colonies *Commun Psychopharmac* **2** 151–157, 1978
6 Ellinwood, E H Jr , A Sudilovsky and L M Nelson Evolving behavior in the clinical and experimental amphetamine (model) psychosis *Am J Psychiat* **130** 1088–1092, 1973
7 Ellison, G , M S Eison and H S Huberman Stages of constant amphetamine intoxication delayed appearance of abnormal social behavior in rat colonies *Psychopharmacology* **56** 293–299, 1978
8 Gambill, J D and C Kornetsky Effects of chronic d-amphetamine on social behavior of the rat implications for an animal model of paranoid schizophrenia *Psychopharmacology* **50** 215–223, 1976
9 Ho, B T and M McKenna Discriminative stimulus properties of central stimulants In *Drug Discrimination and State Dependent Learning*, edited by B T Ho, D W Richard III and D L Chute New York Academic Press, 1978, pp 67–78
10 Humphreys, A P and D F Einon Play as a reinforcer for maze-learning in juvenile rats *Anim Behav* **29** 259–270, 1981

11 Lammers, A J and J M Van Rossum Bizarre social behaviour in rats induced by a combination of a peripheral decarboxylase inhibitor and dopa *Eur J Pharmac* **5** 103–106, 1968
12 McKenzie, G M Apomorphine-induced aggression in the rat *Brain Res* **34** 323–330, 1971
13 Meaney, M J and J Stewart A descriptive study of social development in the rat *(Rattus norvegicus) Anim Behav* **29** 34–45, 1981
14 Miczek, K A Intraspecies aggression in rats effects of d-amphetamine and chlordiazepoxide *Psychopharmacologia* **39** 275–301, 1974
15 Miczek, K A and H Barry, III Pharmacology of sex and aggression In *Behavioral Pharmacology*, edited by S D Glick and J Goldfarb St Louis, C V Mosby, 1976, pp 176–257
16 Nelson, L R and G D Ellison Enhanced stereotypies after repeated injections but not continuous amphetamines *Neuropharmacology* **17** 1081–1084, 1978
17 Panksepp, J The regulation of play neurochemical controls *Soc Neurosci Abstr* **5** 172, 1979
18 Panksepp, J The ontogeny of play in rats *Dev Psychobiol* **14** 327–332, 1981
19 Panksepp, J and W W Beatty Social deprivation and play in rats *Behav Neural Biol* **30** 197–206, 1980
20 Post, R M Intermittent versus continuous stimulation effect of time interval on the development of sensitization or tolerance *Life Sci* **26** 1275–1282, 1980
21 Valzelli, L , Giacalone, E and S Garattini Pharmacological control of aggressive behavior in mice *Eur J Pharmac* **2** 144–146, 1967