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# Play Behavior and Stress Responsivity in Periadolescent Offspring Exposed Prenatally to Cocaine

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WOOD, R. D., V. A. MOLINA, J. M. WAGNER AND L. P. SPEAR. *Play behavior and stress responsivity in periadolescent offspring exposed prenatally to cocaine.* PHARMACOL BIOCHEM BEHAV **52**(2) 367-374, 1995.—Play behavior and stress responsiveness were examined in offspring exposed gestationally to cocaine. The subjects were offspring of Sprague-Dawley rat dams given SC injections of 40 mg/kg/3 cc cocaine HCl daily from gestational days 8-20 (C40), pair-fed dams injected daily with saline (PF), and untreated control dams (LC). Periadolescent (postnatal day (P) 30-36) male and female rats were assigned to either pretest Stress or No Stress conditions. Every other day Stress animals were exposed to a stressor (on P30—foot shock; P32—white noise; P34—forced swim; P36—foot shock), with each stressor being administered 4 h prior to a play session. Immobility during one of the stressors, foot shock, was used to assess stress responsiveness. Play sessions consisted of pairing each experimental animal with a same-sex, nonexperimentally manipulated conspecific for 7 min. The results indicated that periadolescent offspring exposed gestationally to cocaine differed from controls in their stress responsivity, as evidenced by a failure to show increased immobility during the final foot shock session. Also, while cocaine-exposed juveniles did not differ from controls in their own play behavior, these offspring elicited less play solicitation from conspecifics, as evidenced by an increased latency to be pounced, and decreased frequency and duration of being pounced. These findings parallel earlier evidence for altered stress responsiveness in adult cocaine-exposed rats and also suggest that prenatal exposure to cocaine results in altered social cues.

Developmental toxicology  Cocaine  Stress  Play behavior  Periadolescence

PRENATAL exposure to cocaine has been associated with deficits in the areas of social interaction. For instance, Wood and colleagues have shown that adolescent rats exposed gestationally to 40 mg/kg cocaine show significantly less play behavior, as measured by pinning, than controls (22). In adulthood, rats exposed gestationally to cocaine have been shown to be more aggressive toward an intruder (7). Clinically, Chasnoff has suggested that children of cocaine-using mothers may elicit less care from their caregivers due to their frequent irritability and hyperarousal by environmental stimuli (4). Further, Rodning and colleagues have reported deficits in play behavior in children exposed prenatally to cocaine and/or PCP as evidenced by decreased representational play (15). These researchers have also reported less secure attachment to caregivers in these prenatally drug-exposed children (14). However, as subjects in the latter two studies were exposed to other drugs of abuse as well as cocaine, these results may reflect altered social function as a result of a variety of prenatal insults rather than due to a specific action of cocaine.

Prenatal cocaine exposure has also been associated with alterations in later stress responsivity. For instance, adult offspring of dams administered cocaine during pregnancy exhibited significantly less immobility (a characteristic response to environmental stressors) than controls both during exposure to acute stress as well as in the open field testing conducted 24 h following acute foot shock exposure (11). Similarly, adult offspring prenatally exposed to cocaine have been observed to exhibit significantly less immobility during a Porsolt swim test (3) and to fail to show sensitization to foot shock following a prior experience with foot shock (16). In terms of the clinical

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literature, children exposed in utero to cocaine have been reported to exhibit increased startle reactivity and lowered cortisol levels in response to stressors (1,10).

These data, therefore, suggest that fetal cocaine exposure may result in alterations in terms of how offspring interact with others as well as their environment. The purpose of the present study was to examine the consequences of prenatal cocaine exposure followed by experience with postnatal stressors on one index of social behavior that is elicited with high frequency during adolescence—play (12). A further aim of this study was to examine behavioral response to the foot shock stressor in these offspring, as stress reactivity of cocaine-exposed offspring has been examined only in adult animals in the work published to date.

## METHOD

### *Subjects*

The subjects were offspring of Sprague–Dawley VAF dams (Charles River, Wilmington, MA). Animals were housed in a temperature-controlled colony room on a 12 L : 12 D cycle (lights on at 0700 h). Following a 2-week period of acclimation to the colony room, dams were handled for 5 min once daily for 5 days. On the last 2 days of handling, females were injected subcutaneously (SC) with 0.9% saline to acquaint them with the injection procedure. Breeding procedures consisted of placing the females individually with a male at 1700 h and removing the females at approximately 0900 h the following morning. Gestational day 1 (E1) was considered the day when a sperm plug was detected. On E1, all females were assigned as either experimental or surrogate foster (FOS) dams and were housed in breeder cages with ad lib access to pellet (FOS dams) or powdered (experimental dams) lab chow and water.

On E8, experimental dams were assigned to one of three prenatal conditions: cocaine (C40), lab chow (LC), or pair fed (PF). The C40 condition consisted of daily SC injections of 40 mg/kg/3 cc cocaine HCl between E8 and E20. Dams in the PF group were injected SC daily with 0.9% saline from E8–E20. In addition, females in this group were given only as much powdered lab chow and water on a given gestational day as a weight-matched partner in the C40 group. Dams in the LC condition were allowed ad lib access to lab chow and water and were not injected. Body weights and food and water intakes for each experimental dam were recorded daily from E8 to the end of gestation.

Births were checked daily and the day of birth was considered postnatal day 0 (P0). On P1, litters derived from C40, LC, and PF dams were weighed, sexed, and culled to 8–10 pups. Pups were then fostered by litter to recently parturient FOS dams. Four offspring (two male, two female) from each of 10 litters per prenatal treatment group were examined in this study, with the remaining offspring being used in other experiments.

### *Procedures*

At P21, offspring were weaned from their mothers and housed in same-sex sibling pairs in hanging wire cages with ad lib access to lab chow and water. Beginning on P29, the animals to be used in this study were housed in isolation for approximately 27–29 h prior to each play session as described in detail below. At this time, one male and one female from each litter were assigned to each of the two experimental conditions: Stress or No Stress. Using the procedure outlined below, all animals were tested for play behavior every other day from P30 to P36, an age range during which peak levels of play behavior are observed in rats [e.g., see (12)]. In addition, animals in the Stress condition were exposed to a stressor 4 h prior to assessment of play behavior on each of the 4 test days (P30, 32, 34, 36); the specific stressors used are summarized in Table 1. These particular stressors (foot shock, forced swim, and white noise) were selected to represent a range of stressors typically used in stress research. Because repeated exposure to the same stressor often results in some degree of hormonal or behavioral adaptation [i.e., see (2,8,9,18)], the stressors were varied to reduce the possibility that animals would develop adaptation to the stressor exposure during the course of the test sessions. The purpose of administering the same stressor—foot shock—on the first and last day of testing was to examine responsiveness to this stressor both before and after repeated stressor administration. Animals in the No Stress group were not manipulated prior to examination of play behavior on any of the test days.

For assessment of play behavior, each experimental animal was placed into a test chamber with a same-sex, same-age untreated play partner. The untreated colony animals used as play partners were derived from the general breeding stock in our colony; these untreated play partners received the same weaning and housing procedures as experimental animals but were otherwise unmanipulated. Prior to being tested for play behavior, animals from the experimental group were marked along the back for identification. All play behavior testing occurred during the dark cycle, between approximately 2000 and 2200 h. The test chamber, consisting of a 50 × 25 × 30 cm glass container with wood shavings on the floor, was located in a test room separate from the colony room. The testing room was illuminated with dim red light and a videocamera was positioned 3 feet away from the play chamber to record play behavior. Immediately upon placing the play dyad in the test chamber, the behavior of the dyad was recorded for 7 min. Following testing, both pups were removed from the play chamber and placed in their home cages in their original same-sex sibling pairs for the night. The purpose of rehousing the animals in sibling pairs was to avoid potential adverse effects of extended isolation in these young animals. The following day, all animals were isolated at approximately 1700 h prior to play testing the next day (i.e., animals received approximately 27–29 h of isolation prior to play testing). This manipulation was performed to facilitate play, as social isolation has been shown to result in high rates of play (13).

Play behavior was scored from the videotapes using a computerized data collection program by trained observers blind with respect to prenatal condition. Each play session was scored for each animal in the dyad in terms of latency, frequency, and duration of two play behaviors: pinning and pouncing. Pinning was defined as one animal rolling the other over onto its back. Pouncing, a measure of play solicitation, was defined as a dorsal cross by one animal across the other's back.

In addition to play behavior, a second dependent variable recorded for animals in the Stress group was the cumulative time spent immobile during the intershock interval for both the initial shock session, on P30, and the final shock session, on P36. Immobility, a characteristic stress response (2,21), was defined as the absence of all movement except breathing and was scored with a stopwatch by an observer in the testing room. As with the play behavior scoring, all observers were blind with respect to prenatal condition.

TABLE 1
STRESSORS

| Age: | 30 | 32 | 34 | 36 |
|---|---|---|---|---|
| Stressor: | Footshock | Forced Swim | White Noise | Footshock |
| Procedure | 1 mA 1 s shock on FI 60 s schedule for 10 min | 4 min swim in 28°C water | 80 Hz intermittently for 1 h | 1 mA 1 s shock on FI 60 s for 10 min |

## RESULTS

### *Maternal/Litter Data*

An analysis of variance on the percent gain in body weight during pregnancy showed a significant main effect of prenatal treatment, $F(2, 27) = 4.68$, $p < 0.05$. Tukey's tests revealed that females in the PF group gained significantly less weight than females in both the LC and C40 groups (see Table 2). A 3 × 20 (prenatal treatment × days) repeated measures analysis of variance for body weights across gestational days resulted in a significant main effect of days, $F(19, 153) = 763.27$, $p < 0.01$, and a significant interaction of prenatal treatment × days, $F(38, 513) = 5.53$, $p < 0.01$. Tukey's tests showed only that PF females weighed significantly more than females in the LC group from E1 to E3. These differences appear to have occurred prior to the onset of the prenatal treatment regimen and, thus, are the result of an inadvertent sampling bias. No significant differences were found between the three groups of females in terms of gestational length.

TABLE 2
MATERNAL-LITTER SUMMARY DATA (±SEM)

| | LC | PF | C40 |
|---|---|---|---|
| Number of litters | 10 | 10 | 10 |
| Percentage gestational weight gain | 39.88 | 31.64* | 35.49 |
| | (2.11) | (2.24) | (1.17) |
| Food intake (grams chow) | 26.28 | 23.64† | 23.52† |
| | (0.77) | (0.77) | (0.54) |
| Water intake (ml) | 56.81 | 52.26 | 56.76 |
| | (1.84) | (1.69) | (2.30) |
| Gestational length (days) | 22.80 | 22.60 | 22.80 |
| | (0.20) | (0.22) | (0.13) |
| Litter size | 13.3 | 15.0 | 15.5 |
| | (0.70) | (0.61) | (0.52) |
| Number pups in litter | | | |
| Males | 6.80 | 6.40 | 8.00 |
| | (0.90) | (0.67) | (0.39) |
| Females | 6.30 | 8.30 | 7.30 |
| | (0.79) | (0.67) | (0.56) |
| Offspring body weights on Postnatal day 1 (g) | | | |
| Males‡ | 7.68 | 7.56 | 7.08 |
| | (0.20) | (0.20) | (0.22) |
| Females | 7.37 | 7.27 | 6.71 |
| | (0.26) | (0.18) | (0.22) |

*Significantly different from LC and C40 group ($p < 0.05$).
†Significantly different from LC group ($p < 0.05$).
‡Males weighed significantly more than females ($p < 0.01$).

No significant differences were found in the number of male and female offspring per litter. A 3 × 2 (prenatal treatment × sex) ANOVA showed a significant main effect of sex on litter means of male and female body weights at P1, $F(1, 27) = 36.26$, $p < 0.01$, with male offspring weighing significantly more at P1 than females.

### *Time Spent Immobile During Stressor*

A 3 × 2 × 2 (prenatal treatment × sex × days) ANOVA on the cumulative time spent immobile during the intershock interval on the first and final shock days revealed a significant main effect of prenatal treatment, $F(2, 44) = 3.24$, $p < 0.05$, a significant effect of days, $F(1, 44) = 43.66$, $p < 0.001$, and a significant prenatal treatment × days interaction, $F(2, 44) = 4.98$, $p < 0.05$. Subsequent Tukey's tests revealed that animals in the C40 group, while not differing from the LC and PF groups in time spent immobile during the initial shock session, failed to show the increased immobility during the final shock session that was evident in the LC and PF groups (see Fig. 1a). Indeed, when expressed as percent change in immobility from the first to the last foot shock session, a 3 × 2 (prenatal treatment × sex) ANOVA showed that cocaine-exposed offspring differed significantly from the LC and PF groups, $F(2, 44) = 4.71$, $p < 0.05$ (see Fig. 1b).

### *Play Behavior*

All play data were analyzed via separate 3 (treatment) × 2 (sex) × 2 (stress) × 4 (days) ANOVAs, with Tukey's post hoc analyses being used to analyze further significant effects. Data were separately analyzed for the experimental animals and their untreated play partners. For the latter analyses conducted in the untreated play partners, treatment and stress refer to the prenatal treatment and stress condition of their paired experimental partners. For all data, the litter was used as the unit of analysis.

*Number of pins.* Analysis of variance on the experimental animals revealed only a significant main effect of days, $F(3, 120) = 4.86$, $p < 0.005$, with Tukey's post hoc analysis showing that all animals played significantly more on the second day of testing than on the first and final days ($ps < 0.05$) (see Table 3). No significant differences were found in the play partner animals.

*Latency to pin.* The ANOVA for the experimental animals found a significant main effect of sex, $F(2, 39) = 4.36$, $p < 0.05$, with males exhibiting a longer latency to pin a play partner than females (see Table 4). There was also a main effect for days, $F(3, 117) = 4.36$, $p < 0.01$, with animals having a higher latency to pin on the first than on the second day of testing. A similar analysis of latency to pin for the untreated play partners revealed a significant main effect of days, $F(3, 117) = 5.57$, $p < 0.005$. Tukey's post hoc analyses revealed that these animals had a significantly longer latency

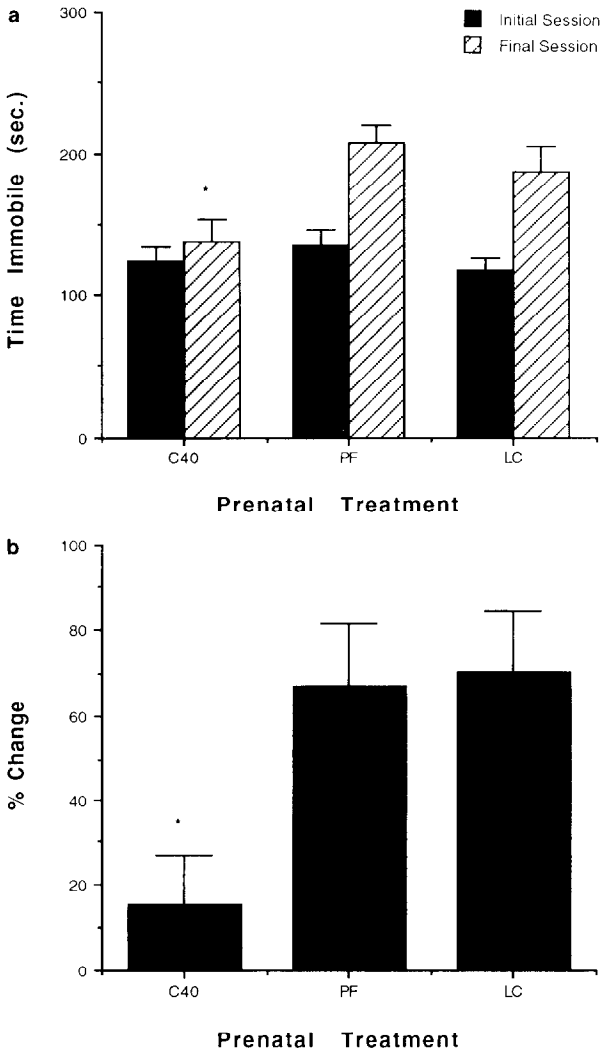


FIG. 1. (a) Mean time (s ± SEM) spent immobile during initial and final foot shock sessions (C40 = cocaine treatment group, $n$ = 15; PF = pair-fed control group, $n$ = 20; LC = nontreated control group, $n$ = 15). *Significantly different from PF and LC, $p < 0.05$. (b) Mean percent (±SEM) change in immobility from initial to final foot shock session (C40 = cocaine treatment group, $n$ = 15; PF = pair-fed control group, $n$ = 20; LC = nontreated control group, $n$ = 15). *Significantly different from PF and LC, $p < 0.05$.

to pin on the first day of testing (P30) than on any other test day ($ps < 0.05$).

*Duration of pin.* For the experimental animals, there was a significant main effect of sex, with females showing a longer pin duration than males, $F(1, 40) = 4.96, p < 0.05$ (see Table 5). There was also a significant main effect of days, $F(3, 120) = 4.81, p < 0.005$; post hoc analyses showed that pin duration was shorter on the first day than on any other. There was also a significant sex × stress × day interaction, $F(3, 120) = 2.81, p < 0.05$. Tukey's test on this interaction revealed only that No Stress females showed a significantly longer pin duration on the second day of testing (mean ± SEM = 18.22 ± 5.72) than on the first test day (4.95 ± 1.69) and also showed

TABLE 3

FREQUENCY OF PINS (±SEM)

| Days | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Experimental | | | | |
| Male | 2.31 | 4.76* | 4.52 | 2.93 |
| ($n$ = 29) | (0.6) | (1.0) | (1.2) | (0.9) |
| Female | 4.22 | 7.83* | 5.61 | 6.09 |
| ($n$ = 23) | (1.0) | (1.9) | (1.5) | (1.1) |
| Play partner | | | | |
| Male | 3.69 | 6.62 | 4.72 | 3.59 |
| ($n$ = 29) | (0.9) | (1.3) | (1.0) | (0.9) |
| Female | 4.48 | 5.78 | 6.13 | 4.74 |
| ($n$ = 23) | (0.7) | (1.3) | (1.6) | (0.8) |

*Significantly different from first and fourth test days ($p < 0.005$).

a longer pin duration on the second day than males in the No Stress group (5.1 ± 2.04). For the play partners, there was a significant main effect of days on pin duration, $F(3, 120) = 3.38, p < 0.05$, with pin duration being shorter on the first day of testing then on the second day.

*Number of pounces.* Analysis of variance on the number of pounces by experimental animals showed a significant sex × day interaction, $F(3, 117) = 2.69, p < 0.05$, with females showing significantly more pouncing on the last day of testing (P36—mean and SEM = 45.5 ± 9.1) than males (31.07 ± 6.21). For the play partners, a significant main effect of Treatment was found, $F(2, 40) = 4.89, p < 0.05$. Tukey's test revealed that play partners playing with animals in the COC prenatal group showed significantly fewer pounces than partners playing with PF and LC animals (means ± SEMs, LC = 29.16 ± 1.9; PF = 31.97 ± 2.2; C40 = 21.59 ± 2.1).

*Latency to pounce.* No significant differences were found in latency to pounce for animals in the experimental group. However, for the play partners, there was a significant main effect of treatment, $F(2, 39) = 3.63, p < 0.05$, with partners playing with animals in the COC group showing a significantly longer latency to pounce than partners playing with LC and PF animals (see Fig. 2). There was also a significant sex ×

TABLE 4

LATENCY TO PINS (S ± SEM)

| Days | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Experimental | | | | |
| Males | 325.7* | 244.3 | 267.4 | 283.7 |
| ($n$ = 29) | (30.1) | (33.5) | (35.8) | (38.9) |
| Females | 263.6*† | 162.0† | 192.4† | 151.0† |
| ($n$ = 23) | (32.6) | (32.5) | (41.0) | (36.1) |
| Play partner | | | | |
| Males | 326.9‡ | 175.4 | 236.2 | 212.3 |
| ($n$ = 29) | (28.3) | (33.1) | (35.0) | (35.5) |
| Females | 262.6‡ | 203.3 | 178.4 | 169.6 |
| ($n$ = 23) | (30.3) | (34.0) | (35.9) | (35.4) |

*Significantly different from second test day ($p < 0.01$).
†Significantly different from experimental males ($p < 0.05$).
‡Significantly different from all other test days ($p < 0.005$).

TABLE 5

PIN DURATIONS (S ± SEM)

| Days | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Experimental | | | | |
| Males | 2.90* | 7.64 | 8.12 | 4.06 |
| ($n$ = 29) | (0.7) | (1.6) | (2.5) | (1.2) |
| Females | 5.75*† | 14.08*† | 12.28† | 14.21† |
| ($n$ = 23) | (2.9) | (3.3) | (3.4) | (2.7) |
| Play partner | | | | |
| Males | 6.20‡ | 13.73 | 10.26 | 5.72 |
| ($n$ = 29) | (1.6) | (2.8) | (2.4) | (1.5) |
| Females | 7.88‡ | 11.43 | 11.58 | 10.44 |
| ($n$ = 23) | (1.7) | (2.7) | (2.4) | (1.9) |

*Significantly different from all other test days ($p < 0.005$).
†Significantly different from experimental males ($p < 0.05$).
‡Significantly different from second test day ($p < 0.05$).

stress interaction for these animals, $F(1, 39) = 4.36$, $p < 0.05$, with the untreated partners playing with Stress females (mean ± SEM = 61.5 ± 17) and No Stress males (59.72 ± 11.4) showing a significantly longer latency to pounce than No Stress females (34.98 ± 5.0) and Stress males (36.63 ± 4.4).

*Duration of pouncing.* For the experimental animals, a significant main effect of stress was found, $F(1, 40) = 5.57$, $p < 0.05$, in which Stress animals (mean ± SEM = 43.65 ± 2.73) showed a greater duration of pouncing than No Stress (36.38 ± 2.17) animals. A significant interaction was found of treatment × sex, $F(2, 40) = 5.11$, $p < 0.05$, in that females in the PF condition had a significantly longer pounce duration than PF males, an effect that was not seen in the other prenatal groups (Fig. 3a). There was also a significant treatment × days interaction, $F(6, 120) = 2.39$, $p < 0.05$, in that COC animals had a shorter duration of pouncing than PF animals on the second day of testing (Fig. 3b).

For the play partners, a significant main effect of treatment was found, $F(2, 40) = 4.14$, $p < 0.05$. Tukey's test revealed that partners playing with COC animals showed a significantly shorter pounce duration than partners playing with LC and PF animals (see Fig. 2).

## DISCUSSION

The data presented in this study suggest alterations in social function in young rats as a consequence of prenatal exposure to cocaine, as has been previously reported (22). Specifically, cocaine-exposed offspring elicited less play solicitation (pouncing) from conspecifics, had a longer latency to be approached for play solicitation, and were pounced upon by their play partners for a shorter duration than controls. The fact that the play differences seen in this study were manifested in how other animals played with cocaine-exposed offspring rather than in alterations in the play behavior of these offspring themselves suggests that prenatal exposure to cocaine is somehow associated with decreased attractiveness to conspecifics. Further research is needed to determine the underlying factors that may promote this apparent unwillingness of other animals to approach cocaine-exposed offspring to play. Wood and colleagues have previously reported significant alterations in the play behavior of cocaine-exposed offspring themselves, as evidenced by lowered rates of pinning (22). It is unclear why this effect was not replicated in the present study, although methodological differences may be one reason. In the earlier study, animals played in a test chamber located within the colony room while the current study assessed play behavior in a testing room separate from the colony. Also, cocaine-

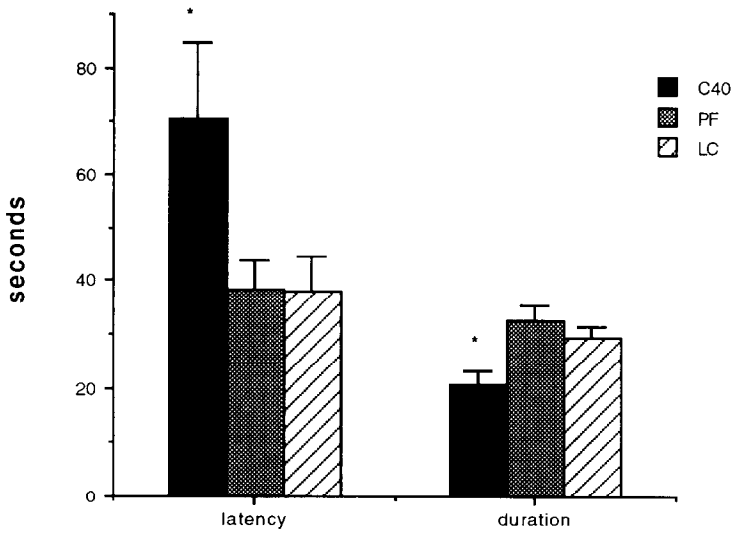


FIG. 2. Mean (±SEM) latency to pounce and duration of pouncing (s) in a 7-min session by play partners paired with experimental animals (C40 = cocaine treatment group, $n$ = 16; PF = pair-fed control group, $n$ = 17; LC = nontreated control group, $n$ = 18). *Significantly different from LC and PF ($p < 0.05$).

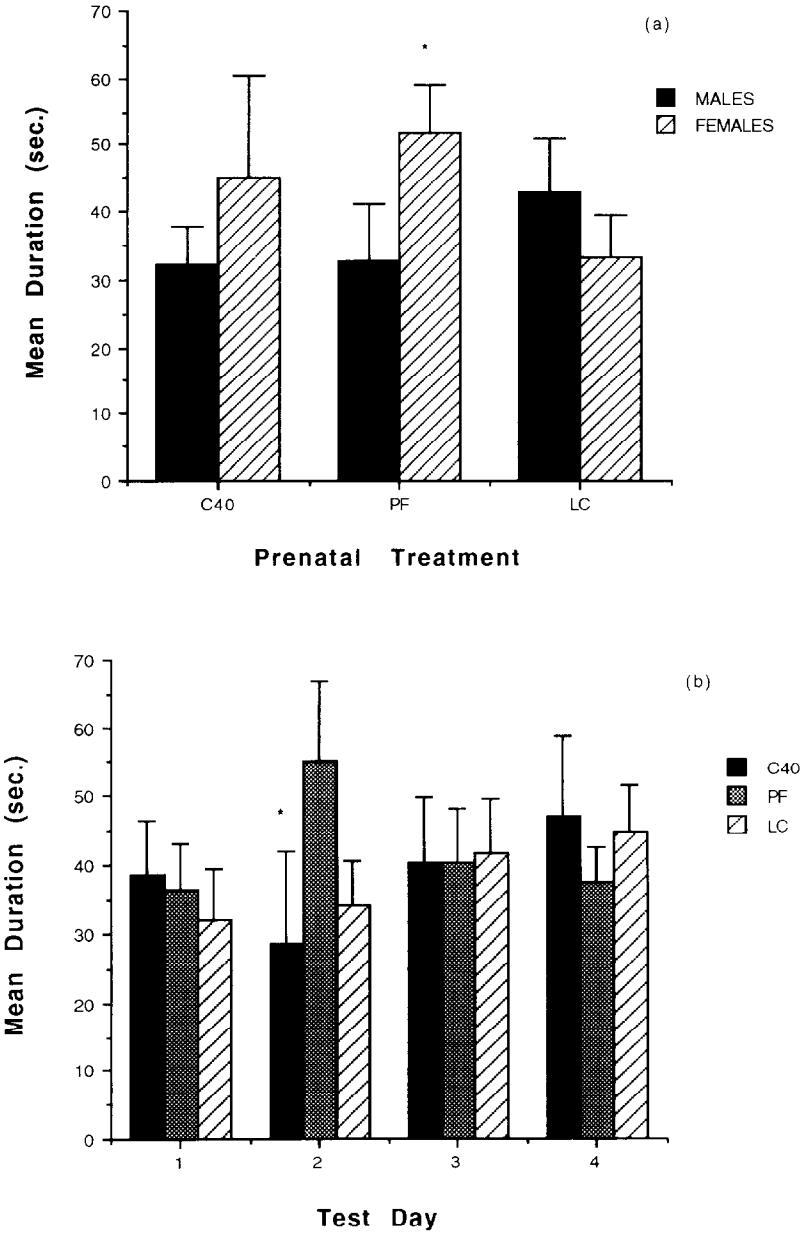


FIG. 3. (a) Mean (±SEM) duration (s) of pouncing by males and females during a 7-min session. *Significantly different from males, $p < 0.05$. (b) Mean (±SEM) duration (s) of pouncing by animals in the three prenatal treatment groups across test days. (C40 = cocaine treatment group, $n = 16$; PF = pair-fed control group, $n = 17$; LC = nontreated control group, $n = 19$). *Significantly different from PF group, $p < 0.05$.

exposed and control offspring in the earlier study received more handling prior to weaning and different group-housing procedures than in the present study. Thus, differences in familiarity with the surrounding environment as well as housing and handling may explain the differences in these studies. It remains clear, however, that social behavior as measured by play is significantly altered in offspring exposed gestationally to cocaine.

Postnatal stress had surprisingly little effect on play behavior either in cocaine-exposed or control offspring. Exposure to one of a variety of stressors presented 4 h prior to each play session resulted only in an increased duration of pouncing (play solicitation), a longer latency of play partners to pounce stressed than nonstressed females, and a shorter latency of play partners to pounce stressed than nonstressed males. Also, although prenatally cocaine-exposed animals differed markedly from controls in their response to repeated stress as assessed by the amount of foot shock-induced immobility emit-

ted during the final stressor exposure, there were no interactions of prenatal treatment with postnatal stress in the play paradigm. One possibility for the generally nonrobust effects of stress on play is that play behavior may be relatively impervious to the effects of stress. The literature supports this viewpoint. For example, Takahashi and colleagues noted that foot shock during a play bout was associated with a slight increase in pouncing and a longer latency to pounce on the day following the initial presentation of shock; however, there was little effect of the stressor on play during the initial session (19). As there were no unshocked controls in the latter study, it is difficult to say whether the observed increase in pouncing reflected a delayed response to the stressor or was indicative of the normal ontogeny of play behavior, which begins to increase at around the age examined (P28) (12). Another possibility may be related to the common procedure of isolating animals for 24 h prior to testing. Although this manipulation is performed to increase rates of play during the test period (13), it is possible that isolation itself may be a notable stressor. As such, the high rates of play in these animals could represent a response to the stress of isolation, and additional stressors might have little impact on an isolation-induced "ceiling effect" on play rates. In fact, it has been suggested that observation of undisturbed social groups (with no prior isolation) may provide a more useful baseline for examination of manipulations that increase play (20). However, the labor-intensive nature of studying play in undisturbed groups, which usually takes numerous hours of continuous observation to obtain measurable levels of behavior, represents an impediment to this approach (20).

With respect to stress-responsivity per se in prepubertal cocaine-exposed offspring, significant differences were observed. These differences were manifested as a failure to show a significant increase in immobility during the final stressor (foot shock) when compared with the first stressor (foot shock) in these offspring. This finding is reminiscent of work by Smith and colleagues, in which previous shock exposure sensitized control, but not cocaine adult offspring to later foot shock (16). It is interesting that differences in immobility during foot shock emerged only after repeated stress exposure in young rats in the present study, whereas adult offspring of cocaine-exposed dams exhibited less immobility than control offspring even in response to acute foot shock (11). It is not clear whether these differences across the two studies represent an age-specific effect or could be attributed to differences in experimental methodology. For instance, in the study by Molina et al. (11), twice as many foot shocks were given during the 10-min test period than in the present study. Further work is needed to determine whether these findings represent altered stress responsiveness during the periadolescent period—an age that has not been well-characterized in the animal literature (17).

In summary, prenatal exposure to 40 mg/kg cocaine was associated with decreased attractiveness to a playmate, as evidenced by less play solicitation by conspecifics. Partners were more hesitant and less likely to play with a cocaine-exposed playmate. Also, cocaine-exposed offspring exhibited altered responsiveness to repeated presentation of a variety of stressors as measured by shock-induced immobility. There were no interactions of postnatal stress with prenatal cocaine exposure in the play paradigm. As animals exposed gestationally to cocaine exhibited altered stress responsiveness, one hypothesis for their decreased attractiveness as playmates may be that they react differently to the stress of a novel social situation [i.e., (5,6)], which could cause them to exhibit different cues than normals. Clearly, further research is needed to determine why cocaine-exposed offspring elicit less affiliative behavior from their conspecifics as well as the locus of their altered stress responsivity. Further study of the two major findings reported here and the possible relationships between them may reveal new insights into the consequences of prenatal exposure to cocaine.

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