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Cocaine disrupts pup-induced maternal behavior in juvenile and adult rats

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Abstract

Impaired onset of maternal behavior in first generation rat dams was previously correlated with rearing by cocaine-treated dams and prenatal cocaine exposure. Pup-induced maternal behavior in non-lactating rats has not been examined with regard to cocaine exposure and rearing conditions. First generation male and female juveniles and young adult males reared by cocaine-treated or control dams and prenatally exposed to either cocaine or control conditions were tested for pup-induced maternal behavior at postnatal days 28 and 60. We now report disruptions in pup-induced maternal behavior in both 28 and 60 day old first generation offspring attributable to rearing condition and prenatal cocaine exposure.

Keywords: Pup-induced maternal behavior; Rats; Cocaine; Rearing environment; Prenatal cocaine exposure

1. Introduction

Maternal cocaine abuse during pregnancy has been correlated with generally poor maternal behavior in humans, including higher levels of maternal neglect and poor maternal-infant bonding [14,47,49]. It is probable that drug-induced maternal neglect has detrimental effects on the future social and parental behavior of adult children, especially given that many of these children are also prenatally exposed to cocaine. Previous reports using animal models found that gestational and postpartum cocaine treatment cause significant delays and disruptions in various aspects of early maternal behavior in the treated rat dam [15,16,19,22,24,37,48,53] and that rearing condition as well as prenatal cocaine exposure has detrimental effects on the onset of maternal behavior in next generation female offspring [16].

Pup-induced maternal behavior, historically called pup sensitization or concaveation [28,38,43] is a procedure where both virgin female and male rats may be induced to express parental behavior towards newborn pups through continuous exposure over a period of time. Following multi-day exposure to young (1–5 days old) pups, male and virgin female rats have been shown to exhibit maternal behavior, including licking, touching, retrieval, nest-building, and sometimes in older rats, standing over or lying on pups in a semi-nursing posture [9,38,40,43,44]. These studies have provided interesting clues concerning possible mechanisms underlying specific aspects of maternal behavior and possible links to performance in general social interaction situations. The validity of pup-induced maternal behavior as a modified model of maternal behavior is supported by the overlap in brain regions and pathways implicated in both normal and induced maternal behavior [32,33].

It is important to note that adult male and female pup-induced maternal behavior seems to be largely mediated by the same

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pathways as normal maternal behavior during lactation, but this is not the case in juveniles between 21 and 28 days of age [23]. Though the intact medial preoptic area (MPOA) is essential for postpartum and pup-induced maternal behavior in adult rats [12,39,41], large lesions of the MPOA in adolescents impair retrieval and nest-building behaviors only, rather than all elements of maternal behavior and gender does not seem to play as important a role [23]. Whereas adult females typically exhibit pup-induced maternal behavior faster than adult males, the reverse is true in juveniles, with males typically taking fewer days to exhibit pup-induced maternal behavior compared to females and juveniles of both sexes generally perform it several days faster than adults [2–4,13,22,29,43,52].

Various rodent studies have reported numerous effects of prenatal exposure to cocaine on subsequent adolescent and adult play, social, and aggressive behaviors [22,36,50,51]. To our knowledge, no prior study has examined the differential effects of prenatal cocaine exposure and rearing condition on next generation offspring pup-induced maternal behavior, although we have recently reported differences in postpartum maternal behavior following prenatal cocaine exposure and altered rearing conditions [16]. Since pup-induced maternal behavior has postural and behavioral components similar to play solicitation and social behavior [3,27] it seems reasonable to suggest that cocaine-induced deficits found in those behaviors may subsequently impact pup-induced maternal behavior as well in cocaine-exposed offspring.

The aim of the present study was to assess the effects of prenatal exposure condition (cocaine or control) and/or rearing condition (reared by cocaine-treated or control dam) on the induction of pup-induced maternal behavior in non-lactating offspring as juveniles and adults. We hypothesized that cocaine-exposed and cocaine-reared offspring would display less pup-induced maternal behavior than control offspring and that there would be no significant sex differences in juvenile behavior.

2. Methods

2.1. Subjects

2.1.1. Treatment dams

Following a 2 week habituation period, virgin female (200 g) Sprague–Dawley rats (Charles River, Raleigh, NC) were placed singly with males on a breeding rack until the day a sperm plug was found, designated as gestation day (GD) 0. Gravid females were randomly assigned to one of five treatment or control groups and singly housed and maintained on a 12:12 reverse light cycle (lights off at 0900) for 7 days. They were then transferred to a room with a regular light cycle (lights on at 0700) for the remainder of the experiment, a procedure that generally results in the majority of dams delivering their litters during daylight hours [30].

Dam treatment/control groups included: chronic cocaine (CC), intermittent cocaine (IC), chronic saline (CS), intermittent saline (IS), and untreated (UN) dams. Chronic cocaine and CS dams received subcutaneous (sc) injections twice daily throughout gestation (GD 1–20) on alternating flanks, of 15 mg/kg cocaine HCL (dose calculated as the free base; Sigma Chemical Company, St. Louis, MO) dissolved in 0.9% normal saline (total volume 2 ml/kg), or normal saline (0.9%) respectively, at approximately 0800 and 1600. Intermittent cocaine-treated dams received the same dose and volume of cocaine as the CC dams, except that their injections only occurred on two consecutive days, every 5 days during gestation (GD 2, 3, 8, 9, 14, 15, 20) and on the same respective days during the postpartum period. Intermittent saline-treated dams received normal saline (0.9%) on the same injection schedule as the IC dams. The intermittent schedule was modeled after a previous study examining behavioral effects of prenatal cocaine exposure on offspring [18] and is designed to model intermittent usage patterns in humans. The IC treatment regimen was employed in addition to the CC treatment as previous research indicated differences in maternal behavior following either acute or intermittent cocaine treatment in dams [19,22,24,48,53] accompanied by differences in oxytocin (OT) system dynamics following the different treatment regimens [7,21]. UN dams were weighed and handled daily, but received no drug treatment. All treatment groups had free access to water and food (rat chow), except the CS-treated dams, who were pair-fed to CC dams in order to control for the anorectic effects of cocaine, as previously described [16]. The IC and IS dams were given 50 g of chow daily on injection days so that each group had equal amounts of food, and food consumption was measured for both groups on those days.

2.1.2. Cross-fostering

On the day of parturition, pups were removed from each dam, weighed, counted, and their gender determined before being culled to a litter of four males and four females. Total litter numbers for each group designation ranged from 12 to 16 generally, with a higher number of UNUN litters (28) listed in Table 1, as extra UN dams and pups were needed to provide pups for other experiments although they were not all included in this study. Litters were either returned to their natural mothers or

Table 1
Experimental groups resulting from cross-fostering

		Rearing dam treatment				
		CC	IC	CS	IS	UN
Litter prenatal exposure condition	cc	CCcc (13)	ICcc (13)	CScc (14)	IScc (14)	UNcc (12)
	ic	CCic (12)	Icic (15)	CSic (12)	ISic (14)	UNic (15)
	cs	CCcs (15)	ICcs (14)	CScs (13)	IScs (13)	UNcs (13)
	is	CCis (13)	ICis (13)	CSis (14)	Isis (16)	UNis (12)
	un	CCun (11)	ICun (15)	CSun (16)	ISun (19)	UNun (28)

Note. Capital letters indicate the original or parent dams' treatment; lower case letters indicate the prenatal exposure condition of first generation offspring. Group designations are as follows: chronic cocaine (CC), chronic saline (CS), intermittent cocaine (IC), intermittent saline (IS), or no treatment (UN). The total number of offspring, for each group are listed in parentheses. Group sizes varied as a result of extra breeding for testing purposes and loss of dams for various reasons during the study.