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Naloxone and Play Fighting in Juvenile Rats

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BEATTY, W. W. AND K. B. COSTELLO. *Naloxone and play fighting in juvenile rats.* PHARMAC. BIOCHEM. BEHAV. 17(5) 905–907, 1982.—According to the opioid hypothesis of social attachment opiate receptor blockade should increase the need for social contact. Yet naloxone reduces play fighting [11], a major form of social interaction in young rats. This observation might be reconciled with the opioid attachment hypothesis if it could be shown that naloxone produced compensatory increases in other social activities or if naloxone shortened play fighting bouts without reducing their frequency. In the present experiment naloxone reduced play fighting in a dose-dependent fashion. However, the frequency of play bouts was reduced, their duration unchanged and no compensatory increase in social sniffing and grooming was observed. In addition, naloxone inhibited rearing almost as potently as it affected play fighting.

Naloxone Opioids Endorphins Opiates Play Social behavior

THE opioid theory of social attachment [8,14] envisions that conditions of low brain endorphin activity engage unconditional responses such as distress vocalizations (DVs) that are likely to result in social contact. Social stimulation releases brain opioids [11], which alleviate distress and produce a pleasurable state. One test of this hypothesis is to measure the effects of opioid agonists and antagonists on behavioral and physiological responses to social deprivation. Studies of DVs after social separation provide consistent support for this hypothesis. Thus, central or peripheral injections of morphine or several different opioid peptides reduce DVs in young puppies, guinea pigs and chicks, while the opiate antagonist, naloxone, blocks these opioid effects and increases the frequency of DVs when given alone [5, 8, 9, 13–16].

If the endogenous opiate systems are involved in mediating social attachment, then treatment with opioid antagonists should increase social interaction by increasing the need for social contact or the value of social rewards while morphine and other opioid agonists should have the opposite effect. In agreement with this idea are the results of studies of competition tests in which preference for a food or social reward was assessed in a T-maze. Naloxone increased preference for the social reward while morphine enhanced preference for the food reward [8]. While this is the expected outcome, it is not clear whether changes in choice behavior reflect alterations in the incentive value of the food or the social reward induced by the drugs.

More troublesome for the idea that endogenous opioid systems mediate social attachments are the effects of naloxone and morphine on pinning, a useful indicator of play fighting in juvenile rats [3,10]. Panksepp [8,14] reports that morphine reliably increased the frequency of pinning while naloxone had the opposite effect regardless of whether or not the animals were housed socially or in isolation. This result contradicts the predicted outcome.

In the present experiment, we attempted to determine if this effect of naloxone on pinning could be replicated. In the same context we examined the effects of naloxone on other aspects of social behavior. Two possibilities were examined: (1) Reduced play fighting after naloxone might be more than compensated for by increased social sniffing and grooming, the other major social activity of young rats. (2) Naloxone might increase the motivation for social interaction but at the same time antagonize the reinforcing effects of social rewards. If this were the case, then naloxone might reduce the duration of bouts of play fighting and other social interaction without affecting the frequency of these encounters.

METHOD

Animals

Subjects were 24 male albino rats of a Sprague-Dawley-derived strain bred by the Holtzman Co., Madison, WI, and shipped to the laboratory at 21 days of age. Except during behavioral testing they were caged singly in standard laboratory cages with free access to food and water in an air conditioned animal room that was illuminated from 0700–1900. Behavioral tests occurred between 0900–1200.

Apparatus

The test chamber, a 51×32×47 cm high box, made of plywood painted black with a clear plastic front, was housed in a quiet room (45 dB(A) re: 20 μPascals at the center of the floor of the chamber). The chamber was illuminated by 2–60 W red incandescent light bulbs mounted in desk lamps, 68 cm above the floor of the chamber. This arrangement pro-

TABLE 1

SOCIAL BEHAVIOR AND REARING PER PAIR (MEAN±SEM) NALOXONE (mg/kg)

	0	1	4	10
Pinning	46.3 ± 3.3	41.9 ± 3.8	36.9 ± 4.0†	32.8 ± 4.1‡
Rearing	135.4 ± 4.1	125.5 ± 3.1	118.1 ± 3.5†	119.8 ± 5.3*
Play Fighting				
Bout Frequency	70.4 ± 2.0	61.8 ± 2.9*	55.9 ± 4.2†	51.3 ± 3.2‡
Total Duration (sec)	230.7 ± 9.0	202.5 ± 12.1*	180.1 ± 13.3†	167.0 ± 12.1‡
Bout Duration (sec)	3.3 ± 0.2	3.3 ± 0.2	3.2 ± 0.1	3.3 ± 0.1
Percent of Play Bouts				
≤1 sec	15 ± 2	13 ± 2	14 ± 2	9 ± 1
>1 and ≤5 sec	70 ± 2	72 ± 2	71 ± 2	80 ± 2
>5 sec	15 ± 2	15 ± 2	15 ± 1	11 ± 1
Social Investigation				
Bout Frequency	7.5 ± 0.8	7.5 ± 1.4	8.3 ± 0.9	10.3 ± 1.0
Total Duration (sec)	9.3 ± 0.9	9.7 ± 1.6	12.0 ± 1.6	14.3 ± 2.1
Bout Duration (sec)	1.3 ± 0.1	1.4 ± 0.2	1.5 ± 0.2	1.4 ± 0.1

Significantly different from 0 mg/kg control *$p<0.05$, †$p<0.01$, ‡$p<0.001$.

vided the minimum light necessary to obtain clear videotape recordings.

Procedure

At 24 days of age the rats were habituated individually to the apparatus. Test pairs (N=12) were then formed by random assignment. These pairs remained intact for the duration of the experiment. Starting on Day 25 and continuing for the next 10 consecutive days each pair received a 10 min-long test at the same time each day. Thus all pairs were 23 hr 50 min socially deprived for all tests. On the first two tests no drugs were administered. On the following 8 days both members of each pair received 0, 1, 4 or 10 mg/kg naloxone HCl (Narcan, Endo Labs, expressed as the weight of the salt) IP 10 min before the start of the test session. The drug was dissolved in physiological saline and administered in a volume of 1 ml/kg. The order of drug treatments was counterbalanced, both between and within pairs with the additional constraint that each pair was tested once at each dose before its second test with any dose.

All sessions were videotaped and subsequently scored by a rater who was blind to the drug treatment received by the rats. The following behaviors were scored for each pair: pinning frequency (one rat rolls the other onto its dorsal surface and stands over it), rearing frequency (either rat raises its forepaws at least 1 cm off the floor), frequency, bout duration and total duration of play fighting and frequency, bout duration, and total duration of social investigation. Play fighting was a composite of several behaviors including tail-pulling, pouncing, boxing, wrestling, pinning, and chasing. Although the latter behavior is often considered separately [1], our previous research [3,10] has consistently shown that under the present conditions the frequency, duration and temporal patterning of chasing are highly and positively correlated with other measures of play fighting. A typical play bout begins when one rat pounces at the other which generally leads to mutual wrestling or (occasionally) chasing or (rarely) boxing. Wrestling matches often lead to pins, which might be followed by a brief cessation in social interaction or a reversal as the pinned animal scrambles to its feet and chases or wrestles with its partner. Timing of individual play bouts continued until a clear interruption in the ongoing sequence of play fighting was detected. Bouts of social investigation, which mainly consisted of anogenital sniffing but also included social grooming, were timed in a similar manner.

Data Analysis

Since performance on all measures was reasonably stable at the 0 mg/kg condition and the pattern of drug effects was similar for both blocks of tests, the data were pooled for each dose. For each dependent variable a within-subjects analysis of variance was performed with naloxone dose as the independent variable treating performance by the pair as a single score. Subsequent pairwise analyses were performed if the F ratio from the omnibus analysis reached statistical significance at the 0.05 level.

RESULTS

As seen in Table 1 naloxone depressed both play fighting and rearing. Analysis of the frequency of pins revealed a reliable drug treatment effect, $F(3,33)=13.19$, $p<0.001$. Subsequent analyses showed that both the 4 and 10 mg/kg doses of naloxone reduced pinning, $F(1,11)>17.77$, $p<0.005$, but the difference between 0 and 1 mg/kg conditions fell just short of significance ($p<0.06$). In addition, the difference between the 1 and 10 mg/kg doses was reliable, $F(1,11)=15.84$, $p<0.005$.

Analysis of the total duration of play fighting revealed a similar pattern. Overall, naloxone reduced play fighting,

$F(3,33)=12.68$, $p<0.001$, in a dose-dependent manner. Relative to the control condition all of the naloxone doses depressed play, $F(1,11)>6.17$, $p<0.05$. In addition, both the 4 and 10 mg/kg doses were more effective in suppressing play fighting than the 1 mg/kg dose, $F(1,11)>5.02$, $p<0.05$.

Naloxone reduced play fighting by reducing the frequency of play bouts, $F(3,33)=11.15$, $p<0.001$, without altering the average bout duration or the proportion of very short or very long play bouts. Relative to the saline control condition all naloxone doses reduced the frequency of play bouts, $F(1,11)>7.23$, $p<0.05$, and the 10 mg/kg dose was more effective than the 1 mg/kg dose, $F(1,11)=17.07$, $p<0.005$.

The influence of naloxone on play fighting was closely paralleled by its effect on rearing, a nonsocial behavior, $F(3,33)=4.69$, $p<0.01$. Subsequent analysis showed that both the 4 and 10 mg/kg doses significantly reduced the frequency of rearing responses, $F(1,11)>9.23$, $p<0.05$. By contrast, naloxone tended to increase social investigation but the effect was not reliable, $F<2.67$, $p>0.05$. Both the frequency of bouts and the average bout duration were unaffected by the drug. The number of social investigation bouts was too small to permit a more detailed analysis of the distribution of bout durations.

DISCUSSION

The present findings replicate earlier work [8] demonstrating that naloxone reduces pinning and extend this finding to other measures of play fighting. Left unanswered is why opiate receptor blockade enhances DVs [5, 9, 13, 15, 16] and preference for social rewards [8] but reduces play. The possibility that naloxone might increase social investigation while reducing play was not confirmed in the present study. Likewise, the prediction that naloxone would simultaneously increase the motivation for social contact, but reduce the rewarding effect of social interaction, leading to a reduced duration of individual play bouts was not supported. Naloxone reduced play fighting by reducing the frequency of play bouts without affecting their duration.

Two explanations of the effect of naloxone on play fighting remain tenable. Firts, a complex social behavior such as play may rapidly extinguish in the presence of the receptor antagonist, naloxone, which presumably blocks the reward value of the social activity. Consistent with this notion is the report that naloxone facilitates extinction of a T-maze position habit originally acquired using a social reinforcer [12].

Alternatively, the effect of naloxone on play fighting may reflect a general depression of active motor responding. The present finding that naloxone was almost as effective in reducing rearing as in inhibiting play is consistent with this view. Naloxone consistently reduces social and exploratory activity [4, 6, 7], but its effects on locomotor activity are equivocal. Activity is most often reduced by naloxone when it is assessed in a social context [2,4]. Thus naloxone might reduce play fighting by inhibiting those active motor behaviors that occur in a social context.

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