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Cocaine Increases Isolation-Induced Fighting in Mice

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HADFIELD, M. G., E. A. NUGENT AND D. E. W. MOTT. *Cocaine increases isolation-induced fighting in mice.* PHARMAC. BIOCHEM. BEHAV. **16**(2) 359–360, 1982.—Isolated male mice were treated with IP cocaine (10 or 35 mg/kg), saline, or received no injections. Groups of four identically-treated animals were placed in a small arena where fighting behavior was observed. Cocaine produced a marked dose-dependent increase in fight duration. The results are discussed in terms of possible catecholaminergic mechanisms.

Cocaine Isolation-induced fighting Agonistic behavior Aggression Catecholamines Mice

COCAINE is a powerful central nervous system (CNS) stimulant. As currently reviewed [5], in humans, cocaine significantly reduces total sleeping time, including the rapid eye movement (REM) phase. It produces euphoria, anorexia, perceptual and affective changes at low doses and paranoid psychoses at high doses. In experimental animals, cocaine increases locomotor activity, body temperature, multiple unit activity in the reticular activating formation and several other changes. It elicits stereotyped behavior and, in animals with lesions in the nigrostriatal tract, it induces turning towards the affected side. Food intake is reduced.

Many of cocaine's effects have been attributed to competitive uptake inhibition of catecholamines (CA's) [11]. However, until recently, an *in vivo* effect of cocaine on CA uptake has only been shown in the periphery; but we recently reported that *in vivo* cocaine competitively inhibits the uptake of the major central CA, norepinephrine, into rat brain synaptosomes [6].

Cocaine's effects on brain CA's may have a bearing on aggression since the CA's have been widely implicated in the production of agonistic behavior [2,3]. Significant changes in CA uptake have been reported in various fighting models by ourselves [7,8], Hendley *et al.* [9] and Welch *et al.* [15]. Moreover, there is some evidence that cocaine alters aggressive behavior in animals though the results are equivocal or in conflict depending on the model used [1, 10, 13]. In the present study, we tested the effect of cocaine on fighting behavior in isolated male mice.

METHOD

Subjects were forty-eight ICR male mice received at six weeks of age from Flow Laboratories, Dublin, VA. Then they were isolated for 4–8 weeks in opaque plastic cages of standard size under controlled conditions of temperature, humidity and lighting (12 hr on/12 hr off). They were provided with standard lab chow and water ad lib. All testing was conducted during the late morning—early afternoon between 10:00 and 15:00 hours. The animals were observed in groups of four and the composition of the groups consisted of the same four animals throughout progressive fighting sessions. The resulting twelve groups were tested twice under each of the four different conditions, each member of the group receiving no injection, physiological saline injection, 10 mg/kg cocaine HCl and 35 mg/kg cocaine HCl—all administered in a volume of 1 cc/100 g body weight IP 10 minutes prior to experimentation. All twelve groups were tested in a counterbalanced order with drug and non-drug injections on alternate days. The results were subjected to a repeated measure analysis of variance and a Duncan multiple-range test [4]. Each group of mice was tested on four consecutive weekdays, two weeks in succession. Minute-by-minute fight durations were measured for the 15 minute sessions on a cumulative recorder, after which the animals were returned to their home cages. Fighting was defined as any aggressive bodily contact, specifically, biting, pummeling and upright face to face sparring with paws touching between two or more animals. The fighting arena was constructed of clear Plexiglas (21 cm high and 169 cm^2 unobstructed floor). The arena was washed thoroughly in detergent between sessions.

RESULTS

The overall effect of the drug treatment was highly significant, $F(3,33)=10.05$, $p<0.0001$ (see Fig. 1 for values). The post hoc comparisons revealed that the two control values did not differ ($p>0.05$), that there was more fighting at the 10 mg/kg condition than at the saline condition ($p<0.05$) but not

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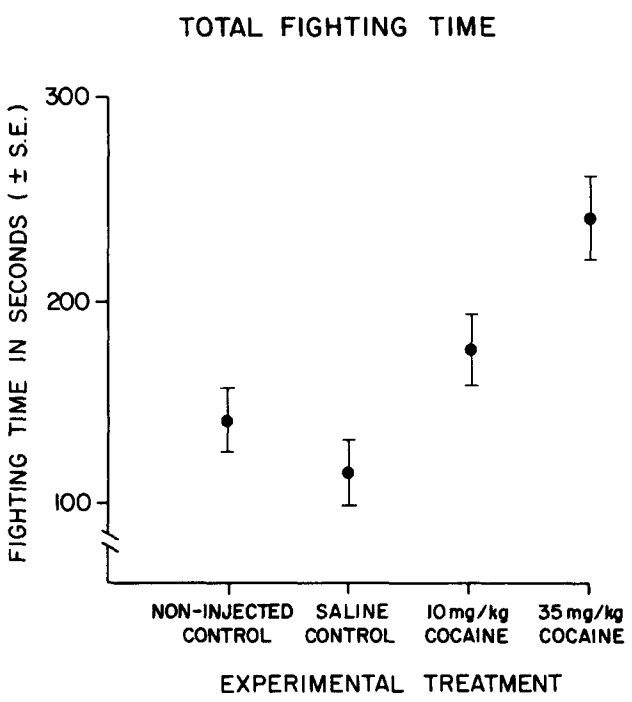

FIG. 1. The effects of two doses of cocaine HCl on the total amount of fighting in previously isolated mice is shown as the mean number of seconds of fighting time. Each point represents the mean of 24 observations of groups of four subjects.

significantly more than at the no injection condition, and that fighting at the 35 mg/kg condition was significantly greater than at all others ($p<0.05$).

DISCUSSION

The cocaine-induced increase in fight duration in our isolated male mice was dose-dependent and striking. The amount of time spent in fighting more than doubled at the highest dose as compared to the saline injection condition. The effect is important because most drugs inhibit fighting behavior in aggressive animals, often by non-specific means such as sedation, etc. [12,14].

Miczek and O'Donnell [13] tested cocaine in the resident-intruder model of aggression and the colony and isolated resident animals attacked the intruder animals less often. Hutchinson *et al.* [10] found variable cocaine effects on aggression, depending on the model, but the ones they used did not include isolation. Brunaud and Siou [1] found that cocaine increased shock-elicited fighting in rats.

The above experimental procedures were quite different from that of the present study and the dosages of cocaine used were lower (0.5–8.0 mg/kg). In our own study, pitting four aggressive isolated animals against one another may increase the opportunity for fighting, since cocaine increases general activity levels (locomotion) and they come into contact with one another more often. Once fighting is precipitated, hyperactivity, coupled with cocaine's anti-fatigue properties may accelerate and sustain the fight. Thus the effect of cocaine on fighting may not be a specific one. However, the effect may be related to CA uptake inhibition produced by cocaine.

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