Naloxone pretreatment enhances shock-elicited aggression

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Pairs of rats were placed in a chamber and given electric shocks of varying intensities in a random order. Two sessions, 48 h apart, were given to each pair. Shock-elicited aggression increased with shock intensity. Pretreatment, before a session, with the opiate antagonist, naloxone, resulted in greater aggression than was evidenced by saline-pretreated controls.

Mammals have evolved central nervous system mechanisms of producing analgesia (Mayer & Price, 1976). This analgesia seems to be mediated, in part, by the action of endogenous opioid peptides (Sherman & Liebeskind, 1979). Recently, we have proposed that one of the functions of this endogenous analgesic system is to prevent nociceptive stimuli from disrupting innate defensive behavior patterns (Bolles & Fanselow, 1980; Fanselow & Bolles, 1979a, 1979b). According to this model, fear-provoking stimuli that trigger defensive behavior should also trigger the endogenous analgesic system. Support for the model comes from findings that show that, in the presence of fear-provoking stimuli, such as innately recognized predators (Blanchard & Blanchard, 1971) or stimuli associated with electric shock (Chance, White, Krynock, & Rosecrans, 1978; Fanselow, 1979; Fanselow & Bolles, 1979b), an animal is more tolerant of nociceptive stimuli. The analgesia produced by stimuli associated with electric shock seems to be mediated by endogenous opiates, since these stimuli increase endogenous opiate activity in the brain (Chance et al., 1978), and the analgesia produced by these stimuli is eliminated by the opiate antagonist, naloxone (Fanselow, 1979; Fanselow & Bolles, 1979b).

We have applied this model to postshock freezing, one of the defensive behaviors of the rat (Fanselow & Bolles, 1979a). As the nociceptiveness of shock is increased, by increasing the current flow through the animal, the amount of postshock freezing likewise increases (Blanchard & Blanchard, 1969; Fanselow & Bolles, 1979a). If endogenous opioid analgesics are being released at the same time the animal is engaging in defensive behavior, then reducing the efficacy of these analgesic substances should increase the perceived nociceptiveness of shock and the rat should evidence more postshock freezing. Support for this hypothesis comes from the finding that the opiate antagonist naloxone increases postshock freezing in a

dose-dependent manner (Fanselow & Bolles, 1979a).

The purpose of the present experiment is to extend this behavioral effect of naloxone to a second defensive behavior, shock-elicited aggression (SEA). When two rats are confined together and shocked, they typically assume an upright posture and "box" (O'Kelly & Steckle, 1939). Blanchard, Blanchard, and Takahashi (1977) found that the behaviors of rats engaged in SEA resemble more closely those of rats forced to enter established rat colonies than those of the dominant alpha males. Therefore, they argued that SEA is actually a defensive behavior. The present experiment demonstrates that the incidence of this defensive behavior, like postshock freezing, increases with both shock intensity and naloxone pretreatment.

METHOD

Subjects

The subjects were 12 adult female rats of Long-Evans descent, reared at the University of Washington, Psychology Department vivarium. The rats weighed between 208 and 242 g. They were housed in individual cages with ad-lib access to food and water. The experiment was conducted during the lights-on portion of a 12:12 h day:night cycle. The rats were grouped into six pairs of animals matched for weight. The mean difference in weight between animals in a pair was 4.0 g (range 1-10 g).

Apparatus

Aggression was observed in a 26×23×24 cm chamber. The ceiling and front viewing wall were made of Plexiglas, and the remaining walls were constructed of stainless steel. The floor was composed of 13 stainless steel rods, 1 cm in diameter and spaced 1.9 cm center to center. Illumination was provided by a 7.5-W white light bulb suspended 5 cm above the ceiling. Scrambled shocks of .5, .6, .8, 1.0, 1.3, 1.6, 2.0, 2.5, 3.0, and 4.0 mA were delivered for .5 sec by a Grason Stadler shock generator/scrambler connected to each of the floor rods and the stainless steel walls.

Procedure

Each pair of rats was given two sessions spaced 48 h apart. A pair was placed inside the chamber, and after 3 min the animals were given 20 shocks (2 of each intensity in a random order) spaced 15 sec apart.

Immediately before each session, the animals were given either an ip injection of naloxone hydrochloride (3 mg/kg) or an equivalent volume of isotonic saline. Both members of a pair were given

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an injection of the same substance immediately prior to the session. Half the pairs received naloxone before the first session, and half received saline before the first session. Each pair received an injection of the other substance before the second session.

An observer, blind to both the intensity of shock and the drug given, scored an instance of aggression if the pair boxed or lunged toward each other during the shock. A second observer, who gave the injections and controlled the programming equipment, provided a reliability check on the blind observer. The two observers agreed on 89% of the observations. Only the data obtained by the blind observer were used in the statistical analyses.

RESULTS

Figure 1 shows the mean number of instances of aggression in the 20 trials of each session following either saline or naloxone pretreatment and collapsed over shock intensity. These data were subjected to a two-factor analysis of variance with a within-subjects factor of saline or naloxone and a between-subjects factor for order (whether saline or naloxone was given before Session 1). There was an overall effect of drug [$F(1,4)=27.79$, $p < .01$]; naloxone increased aggression over saline controls both in Session 1 [$F(1,4)=12.5$, $p < .025$] and in Session 2 [$F(1,4)=15.4$, $p < .025$]. There was also more overall aggression during Session 1 than in Session 2 [$F(1,4)=27.85$, $p < .01$].

Figure 2 shows the relationship between shock intensity and SEA. There was a significant positive relationship between shock intensity and aggression when the subjects were treated with naloxone [$r(8) = .93$, $p < .005$] or saline [$r(8) = .78$, $p < .005$]. Regression lines between shock intensity and aggression were determined for each pair under both saline and

Figure 1. The mean percentage of the 20 shocks that elicited aggression in Session 1 and in Session 2, 48 h later. The white bars indicate pairs that were pretreated with naloxone; the striped bars indicate saline controls.

Figure 2. The mean percentage of aggression at each shock intensity. Closed circles indicate naloxone pretreated pairs; open circles indicate saline pretreated pairs. Each data point represents two determinations for each of the six pairs. The regression lines were determined by the method of least squares.

naloxone by the method of least squares. The slope of the regression line was greater following naloxone pretreatment than following saline [$t(5)=6.35$, $p < .005$], while the y intercepts did not differ reliably [$t(5)=1.58$, $p > .10$]. This pattern of results indicates that SEA increased with shock intensity and that naloxone's enhancement of SEA was most pronounced at the highest shock intensities.

DISCUSSION

Naloxone pretreatment was found to increase SEA, just as it increases a variety of other reactions to a variety of nociceptive stimuli (e.g., Fanselow & Bolles, 1979a; Jacob, Tremblay, & Colombel, 1974; Kokka & Fairhurst, 1977). It is most parsimonious to suggest that the effect of naloxone upon these various behavioral indices of reactivity to nociceptive stimuli is mediated by the antagonistic action of the drug upon the endogenous opiate analgesic system. Naloxone causes nociceptive stimulation to be perceived as more noxious than it would normally be if the analgesic system was unopposed.

The present study confirms an earlier report by Dreyer and Church (1968) that SEA increases with shock intensity. Similarly, Ulrich and Azrin found that SEA increased with shock intensity up to 2 mA but that higher intensities caused a reduction in SEA due to "the debilitating effects of the shock" (Ulrich & Azrin, 1962, p. 515). SEA also increases with shock duration (Azrin, Ulrich, Hutchinson, & Norman,

1964; Dreyer & Church, 1968) and shock frequency (Ulrich & Azrin, 1962). It seems reasonable to conclude that SEA increases with the nociceptiveness of the stimulation. Such a conclusion logically justifies the above hypothesis, that naloxone increased SEA by increasing the apparent nociceptiveness of the shock.

The example of defensive behavior used in the present experiment—shock-elicited aggression—is quite different in topography from the defensive behavior of freezing that was examined in earlier work (e.g., Fanselow & Bolles, 1979b). Shock-elicited aggression occurs immediately with the onset of shock and is an increase in activity, but each bout is short-lived. Freezing has a more gradual onset, slowly increasing after shock offset, and represents a decrease in activity; each bout has a prolonged duration (Bolles & Riley, 1973; Fanselow & Bolles, 1979a). However, both of these topographically different behaviors are most appropriately considered as defensive (Blanchard, Blanchard, & Takahashi, 1977). Thus, similar findings with these two behavioral indices support the contention that endogenous analgesic systems are triggered by fear-provoking stimuli that also trigger defensive behavior (Bolles & Fanselow, 1980; Fanselow & Bolles, 1979a, 1979b).

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