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# Mescaline and Shock Induced Aggression in Rats[1]

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SBORDONE, R. J. AND B. CARDER. *Mescaline and shock induced aggression in rats.* PHARMAC. BIOCHEM. BEHAV. 2(6) 777–782, 1974. – Rats were treated with mescaline and tested in a shock induced aggression situation. Low doses (10 mg) prolonged the bouts in the first experiment, but did not in the second. The topography of the fighting behavior for the animals given this dose was like that of controls. Doses of 50 mg/kg increased the duration of the bouts, and even caused fighting to continue during a five minute period following shock termination. In addition, the topography of the behavior changed. The rats treated with 50 mg/kg of mescaline were initially inactive and unresponsive to shock. After a few shocks, however, these rats engaged in prolonged biting attacks while in a prone position. It was proposed that the higher dose of mescaline induced an experimental catatonia in which normal inhibitory mechanisms that control and limit aggressive behavior are ineffective.

Mescaline Catatonia Shock induced aggression Hallucinogen

CARDER and Olson [4] recently reported that rats treated with marihuana fought more than controls in a shock induced aggression situation. The increase in aggression, however, was only observed in rats that had never received prior exposure either to the drug or the test situation. The authors proposed that the marihuana induced perceptual alterations which combined with a fear of the novel test situation to increase aggressiveness. This hypothesis predicted that other drugs which alter perception, such as mescaline, should also enhance shock induced aggression in rats, providing that the rats had no prior experiences either with the drug or with the test situation.

There are several reports in the literature on the effects of mescaline on aggressive behavior in rodents. The drug has produced increases in spontaneous aggression [8] but decreases in experimentally induced aggression [17]. In the test of the drug on experimentally induced aggression, however, the animals were exposed to the aggression situation before the effects of mescaline were tested in that situation. The present series of studies, therefore, examined the effects of mescaline on shock induced aggression in rats that had no previous exposure either to the drug or the test situation.

## EXPERIMENT 1

### METHOD

*Animals*

Twenty-four experimentally naive, male Sprague-Dawley rats over 90 days old, obtained from the Simonsen Breeding Laboratory, Gilroy, California, were housed separately with food and water available at all times.

*Apparatus*

An experimental chamber (29 X 24 X 20 cm) was used for aggression testing. The two ends were of sheet metal; the sides and the top were of Plexiglas. The floor was made of stainless steel rods spaced 1.25 cm apart. Shocks were delivered to the animals through floor grids from a constant current source operating through a Davis Model 255 grid scrambler. The duration of shock and interval between shocks were automatically controlled by a series of timers.

The aggressive episodes and the delivery of shock were recorded on an Esterline-Angus recorder located in another room. This permitted a paper tape record of the latency and duration of each episode.

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*Procedure*

Each pair of rats was randomly assigned to one of three experimental conditions: in the first each pair received an intraperitoneal injection of distilled water; in the second and third conditions each pair received intraperitoneal injections of 10 mg and 50 mg/kg of bodyweight, respectively of mescaline hydrochloride in a distilled water solution, approximately 20 min prior to aggression testing.

For aggression testing a pair of rats was placed on the grid floor of the experimental chamber. Electric shocks of 1.5 sec duration were given every 30 sec. Five shocks were given at each of 10 intensities in ascending order: 0.8, 1.0, 1.2, 1.5, 1.8, 2.0, 2.2, 2.3, 2.4, 2.5 mA. Aggression episodes were measured by an observer familiar with shock induced fighting who depressed a microswitch when any striking or biting movements were produced by either rat and released it when they terminated. In this study and in Experiments 3 and 4, wrestling was not scored as aggression. Another observer initiated the shock trials, and recorded the physical postures of the animals when they engaged in fighting. Both observers were unaware of the particular drug treatment given a pair of animals though the postural effect of the 50 mg/kg dose may have revealed animals in this treatment condition. Each testing session lasted 25 min.

## RESULTS

When the control rats fought, both animals assumed an upright posture and engaged in a brief fighting episode immediately following the onset of shock. These rats were never observed to bite and rarely fought in the intershock interval. The 10 mg/kg mescaline rats differed from the no-drug controls in that they fought frequently during the intershock interval, but were similar in that they fought in an upright posture and never engaged in biting. The aggressive episodes of the 50 mg/kg pairs differed dramatically from both the no-drug controls and the 10 mg/kg rats. Prior to the onset of fighting these rats adopted a low, flat crouch, were hypokinetic and ataxic. They exhibited little or no reaction to the shock, and generally engaged in no social interaction. When fighting began one rat would suddenly lunge toward the head of the other rat and savagely begin biting its face. These attacks appeared unrelated to the onset of shock. No retaliation was made by the attacked rat. Instead he assumed a variety of submissive postures or attempted to escape from his attacker. None of these behaviors appeared to have any noticeable effect on the violent behavior of the other rat. These episodes often lasted until the arrival of the next scheduled shock temporarily disrupted them. While no systematic attempt was made to determine how long these violent episodes would last, they would often persist until the pair was removed from the test situation.

Table 1 presents the total number of shock induced fighting episodes at each dose level. The data indicate that the 10 mg/kg rats fought more than controls, but this effect did not approach statistical reliability (one factor analysis of variance $F(2,9) = 1.56$, $p<0.25$). Taken alone, however, this particular measure does not present a complete description of the drug's effect on aggression.

Table 2 presents a comparison of the mean duration of individual fights for each drug condition. The data clearly indicate that rats pretreated with mescaline fought longer than controls during the experimental session. A one factor analysis of variance revealed a significant effect attributable to the drug ($F(2,9) = 7.31$, $p<0.02$). Newman-Keuls tests indicated that only the 10 mg/kg group differed from the controls ($p<0.01$). The differences, however, between the controls and the 50 mg/kg group, and between the 10 mg/kg and the 50 mg/kg group approached statistical reliability ($p<0.10$). Figure 1 presents the mean duration of fighting as a function of shock intensity for the three treatment groups. The control group did not fight at all at the lowest intensity, but showed a small, gradual increase in fighting as intensity increased. The mescaline treated rats fought more at all shock intensities, but their behavior was also intensity dependent, with more fighting at the higher shock intensities. With the 10 mg/kg treated animals, maximum fighting occurred at 2.3 mA, less than the maximum shock intensity. This might have resulted from fatigue, since shock intensity was confounded with length of time in the test situation.

Treatment with mescaline increased the latency of attack following the shock. Controls initiated their fights an average of 1.3 sec following shock onset, 10 mg/kg treated rats fought 2.7 sec after shock, and 50 mg/kg treated rats fought 5.8 sec after shock onset. A one factor analysis of variance revealed a powerful effect attributable to the drug ($F(2.9) = 18.74$, $p<0.001$). Newman-Keuls tests indicated

TABLE 1

TOTAL NUMBER OF FIGHTING EPISODES FOR INDIVIDUAL PAIRS IN THREE TREATMENT CONDITIONS

| | Control | 10 mg/kg mescaline | 50 mg/kg mescaline |
|---|---|---|---|
| | 39 | 29 | 31 |
| | 8 | 42 | 15 |
| | 42 | 92 | 48 |
| | 34 | 40 | 10 |
| Mean | 30.75 | 50.75 | 26.00 |
| S.D. | 13.4 | 24.3 | 14.9 |

TABLE 2

MEAN DURATION OF FIGHTING EPISODES FOR INDIVIDUAL PAIRS IN THREE TREATMENT CONDITIONS

| | Control | 10 mg/kg mescaline | 50 mg/kg mescaline |
|---|---|---|---|
| | 0.904 sec | 5.260 sec | 1.400 sec |
| | 0.630 | 2.628 | 1.818 |
| | 1.141 | 3.391 | 4.346 |
| | 0.684 | 3.632 | 1.370 |
| Mean | 0.839 | 3.727 | 2.233 |
| S.D. | 0.517 | 0.825 | 1.233 |

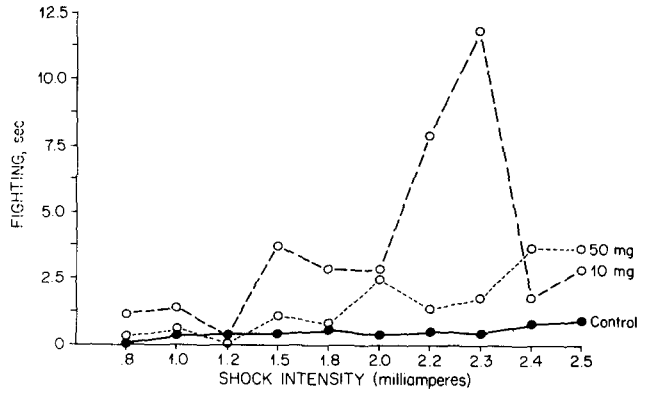


FIG. 1. Mean total duration of fighting at each shock intensity for three treatment groups.

that the 50 mg/kg group differed from both controls and the 10 mg/kg group ($p<0.01$), while the difference between controls and the 10 mg/kg group approached statistical reliability ($p<0.10$).

Treatment with mescaline not only increased the latency and prolonged the duration of fighting, but mescaline treated rats, unlike controls, frequently initiated several fights after a single shock. For the 10 mg/kg treated rats, 52% of their fights occurred after the initial shock induced bout (secondary fights). For the 50 mg/kg treated rats, 40% of their fights occurred after the initial shock induced bout and for the controls the figure is 15%. The increase in secondary fights was statistically reliable (one factor analysis of variance $F(2,9) = 6.52$, $p<0.025$). Newman-Keuls tests indicated that both mescaline groups differed from the no-drug controls ($p<0.05$), but did not differ from each other.

Thus mescaline increased the latency and duration of fighting, and led to the outbreak of fights in the interval between shocks. At the highest dose (50 mg/kg) the drug altered the fighting posture from upright to prone and led to vicious, prolonged biting. The increases in aggression produced by mescaline were different from those produced by marihuana in the same experimental situation [4]. Marihuana increased the frequency of fighting but did not increase the duration of fights and never produced postural changes or biting.

## EXPERIMENT 2

Since previous work [4] demonstrated that marihuana enhanced aggression only during the first test session, we carried out repeated testing with mescaline to further examine its similarity to the effects of marihuana on aggression.

### METHOD

Twenty-four naive, male Sprague-Dawley rats over 120 days old, obtained from the Simonsen Breeding Laboratory, were used. The apparatus was the same as that used in the previous study. The procedure differed in two respects from the previous study, but was otherwise identical. The differences were: (1) animals were observed for 5 min before onset of the first shock and 5 min after the termination of the last shock. (2) Aggression, in this study only, was scored whenever the rats pushed, wrestled, boxed or bit each other. In the other studies reported here, only boxing and biting were scored as aggression.

Rats were divided into 4 groups of 3 pairs each. One group was a water control, the other 3 groups received 10, 20 and 50 mg/kg of mescaline, respectively.

Seven days after the original testing, the rats were again treated with mescaline and tested. Finally, 7 days after the second test, the rats received a third test under mescaline. In these repeated tests, the same pairs were tested together and at the same drug dose as in the original test.

### RESULTS

Figure 2 presents the mean duration of fighting as a function of drug dose for three successive tests. The figure represents fighting which occurred between the onset of the first shock and the termination of the final shock (i.e. fighting during the 5 min pre- and postexperimental periods is not included). Although the behavioral criteria for aggression, the ages of the animals, and the experimental procedure prior to shock were different from the first experiment the data essentially replicate that experiment. Mescaline produced a drug related increase in the duration of fighting during the first testing session (one factor analysis of variance $F(3.8) = 5.29$, $p<0.05$). Newman-Keuls tests indicated that the 50 mg/kg group differed from each of the other mescaline groups and controls ($p<0.05$), while none of the other mescaline groups differed significantly from controls or from each other.

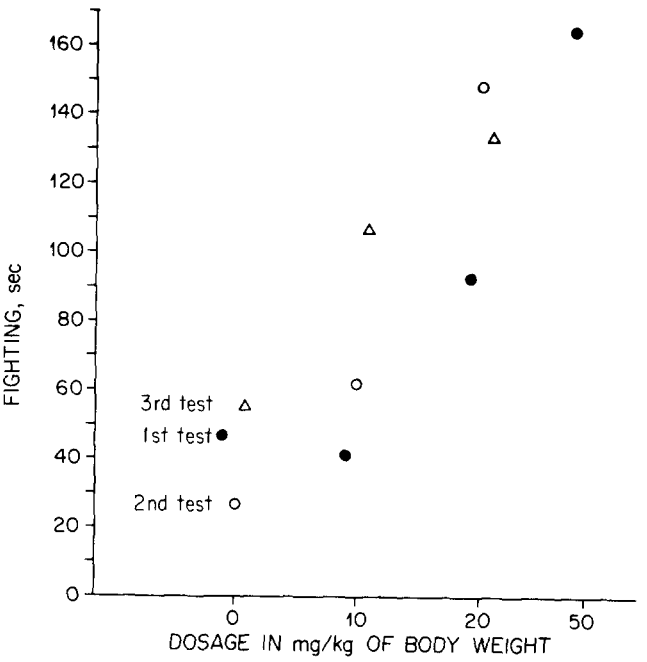


FIG. 2. Mean total duration of fighting as a function of drug dosage for three tests.

Table 3 presents the mean duration of fighting in the 5 min post shock period. Fighting during this period was never observed in control animals, but the data clearly indicate that there is a dose related increase in fighting during this period, which is particularly evident at the 50 mg/kg dose. Fighting during this period was even more

TABLE 3

TOTAL DURATION OF FIGHTING IN FIVE MINUTE POST SHOCK PERIOD FOR INDIVIDUAL PAIRS AS A FUNCTION OF DRUG DOSE

| | Control | 10 mg/kg | 20 mg/kg | 50 mg/kg |
|---|---|---|---|---|
| | 0.0 sec | 0.0 | 23.5 | 2.8 |
| | 0.0 | 0.0 | 0.0 | 303.0 |
| | 0.0 | 0.0 | 4.0 | 226.0 |
| Mean | 0.0 | 0.0 | 9.17 | 177.25 |
| S.D. | 0.0 | 0.0 | 10.26 | 127.33 |

intense for 2 of the 3 50 mg/kg pairs than when shock was delivered. This is further evidence of the potency of mescaline for increasing aggression.

Repeated testing of the animals produced no significant change in the pattern of results. Though the figure suggests an increase in fighting at each dose over successive tests, this effect was not statistically reliable (two-way analysis of variance $F = 2.22$, $p<0.25$). This finding is very different from the previous finding with marihuana in that the results of the initial aggression test under marihuana are quite different from the results of succeeding tests.

It should be noted that observations of rats treated with 50 mg/kg are included for only one week. This was because at least one member of each pair died following the first test at that dose. The cause of death was probably heart failure, as post mortem examination revealed massive congestion of the lungs. Experiments are in progress to determine the relative contribution of the aggression test situation and the drug to these fatalities, but it would appear that the drug alone, in doses of 50 mg/kg should not be fatal. The LD 50 for intraperitoneal administration of mescaline in rats has been found by one group to be as high as 370 mg/kg [10].

## EXPERIMENT 3

In the previous studies, rats tested with 50 mg/kg of mescaline engaged in repeated violent fights while in non-upright postures. It is possible that this violent behavior may have been simply due to the drug's restriction of upright postures, rather than an effect on the central control mechanisms for aggression. For example, other studies have shown that when a rat was paired with a guinea pig and both shocked, the rat assumed the crouched posture of the guinea pig and bit its head [16]. When placed in a narrow tube which restricted movement, rats bit objects in front of them [1]. Placing several rats in a chamber 3 in. high which prevented upright postures resulted in vicious biting attacks which persisted for several hours after the application of periodic shocks [12]. Since these studies are consistent with the idea that the violent behavior produced by 50 mg/kg of mescaline rats in the previous studies may have been due to the drug's restriction of upright postures, we investigated this effect by preventing non-drugged rats from assuming postures during an experimental session.

### METHOD

*Animals*

Six experimentally naive, male Sprague-Dawley rats over 90 days old, obtained from the Simonsen Breeding Laboratory, were housed separately with food and water available at all times.

*Apparatus*

In addition to the apparatus described previously, a sheet of Plexiglas (29 X 20 X 0.75 cm) was fastened to both ends of the experimental chamber and placed approximately 7.5 cm above the grid floor to form a low ceiling. Several holes in the Plexiglas provided adequate ventilation.

*Procedure*

The animals were divided into 3 pairs and were tested in the aggression situation according to the procedure described for Experiment 1. None of the rats received any drug.

### RESULTS

The prevention of upright postures in non-drugged rats during shock induced fighting resulted in biting in 24.1% of the fighting episodes. This biting, however, did not resemble the biting observed in rats dosed with 50 mg/kg of mescaline in that it was very brief, appeared highly correlated with the onset of shock, and never resulted in injury.

Except for the biting, no other difference was found between these rats and the controls in the first experiment with respect to the number, latency and duration of the fighting episodes. These data clearly indicate that while biting may have resulted from the postural effects of the drug, the extreme violence of the fighting episodes observed in rats given 50 mg/kg of mescaline was not due simply to the drug's prevention of upright postures, and may have been due to the drug's activation of central control mechanisms responsible for aggression.

## EXPERIMENT 4

In the first two experiments one member of each pair that was given 50 mg/kg of mescaline would continue to attack the other member despite the latter's submissive postures, cries and attempts to escape. It is not possible to conclude from these studies, however, whether the prolongation of fighting resulted from drug induced changes in the attacker, the victim or both. In order to make a preliminary examination of these possibilities we paired mescaline treated rats with controls. If the mescaline treated rats attacked and fought long bouts with controls this would indicate that drug induced changes in the attacker were crucial while if bouts of normal duration ensued, it would suggest that changes in the victim were crucial.

### METHOD

*Animals*

Twelve experimentally naive, male Sprague-Dawley rats over 90 days old, obtained from the Simonsen Breeding Laboratory, were housed separately with food and water available at all times.

*Apparatus*

The apparatus used in this experiment was exactly as described in the first experiment.

*Procedure*

Rats received intraperitoneal injections of distilled water or mescaline (either 10 mg/kg or 50 mg/kg) approximately 20 min prior to aggression testing. Rats were marked by different colored dyes so that individuals could be distinguished and paired with rats that received different drug treatments to form 3 groups of 2 pairs (water–10 mg/kg, water–50 mg/kg, 10 mg/kg–50 mg/kg). Except for an additional observer who judged which rat initiated and won the aggressive episodes, the aggression testing situation was exactly as described in the first experiment. A rat was judged to have won a bout when its opponent was attempting to escape at the end of the bout. None of the observers were told of the condition to which each rat belonged although the postural effect of the 50 mg/kg dose may have made this treatment evident.

RESULTS

Contrary to our original expectations, the pairing of a 50 mg/kg rat with either a 10 mg/kg or a non-drugged rat resulted in a complete absence of aggressive behavior. On the other hand, 10 mg/kg rats, when paired with non-drugged controls, were found to initiate a high proportion of fights (80.2%), and were judged to have won the majority (62.8%) of them.

## GENERAL DISCUSSION

Mescaline is a very potent facilitator of shock induced aggression in rats. At lower doses (10–20 mg/kg) the drug has properties which suggest a stimulant action: the duration of bouts was increased in Experiment 1, though this effect failed to appear in Experiment 2.

At higher doses, mescaline produced powerful, qualitative changes in aggressive behavior. Pairs of rats that received identical doses of 50 mg/kg engaged in repeated, violent episodes in which a previously docile, ataxic and hypokinetic rat would suddenly lunge at the other rat and inflict deep, injurious bites into its face and mouth despite the latter's submissive postures or attempts to escape. These attacks appeared to be only loosely related to the onset of shock and were apparently not due solely to the drug's prevention of upright postures. While several treatments have been reported to increase shock induced aggression, including septal lesions [3] treatment with rubidium salts [15] and cannabis administration [4], we have found no descriptions in the literature of treatments which produce qualitative changes in aggression such as biting and extreme prolongation of bouts as mescaline does.

In fact the behavior of animals treated with 50 mg/kg of mescaline has a biphasic nature. The animal is inactive, ataxic, cataleptic, and generally unreactive to shock. At some point, however, the behavior dramatically changes to violent attack. This bears at least a superficial similarity to human catatonic patients, who are generally inactive and unresponsive, but who occasionally exhibit brief, unpredictable outbursts of violent behavior [6].

The suggestion that mescaline induces a catatonic state in rats is not new. DeJong [5] has reported that mescaline, in doses of over 25 mg/kg, produces "experimental catatonia" in a variety of animals. This author did not report aggressive behavior in his animals, however. It is possible that in the present experiment, the electric shock, over several presentations, produced a shift in behavior from the inactive to the active mode which would not have developed in the absence of the shocks.

One of the very striking properties of the aggressive behavior of the animals treated with 50 mg/kg of mescaline is that the behavior seems to continue independently of the actions of the victim. The data suggest that mescaline impairs the action of inhibitory mechanisms that normally serve to terminate or reduce the severity of fighting. Bouts are prolonged by the drug, and the severity of the attacks escalates in spite of the apparently submissive behaviors displayed by one member of a pair.

It is possible that drugged rats are unable to assume the appropriate submissive postures to inhibit their opponent's attack. This seems unlikely since the type of posture observed in our 50 mg/kg rats (when they are not attacking) has been described as submissive by a number of investigators [2, 7, 11, 14], and was certainly sufficient to prevent attack by undrugged rats in the fourth experiment. Therefore the most likely way in which mescaline impairs the action of mechanisms which inhibit aggression is by interfering with the drugged rat's ability to perceive a submissive posture and/or respond appropriately.

The preliminary finding that rats treated with 50 mg/kg of mescaline did not fight at all with controls suggests that changes in aggressive behavior induced by this high dose of mescaline result from changes in both attacker and victim. A normal rat will not initiate fighting with a 50 mg/kg treated rat, but another 50 mg/kg treated rat will. Thus the drug causes the attacker to respond to a target that a normal rat will not attack. Likewise a 50 mg/kg treated rat will not attack a normal rat but will attack another 50 mg/kg treated rat. Thus the drug must induce changes in the target to make it susceptible to attack by a mescaline treated animal. These findings are based on only one experiment with few animals but they suggest that work should be carried out in the future to separate the effect of the drug on attack and defense.

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