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Mescaline Produces Pathological Aggression in Rats Regardless of Age or Strain[1]

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SBORDONE, R. J., J. A. WINGARD, M. L. ELLIOTT AND J. JERVEY. *Mescaline produces pathological aggression in rats regardless of age or strain.* PHARMAC. BIOCHEM. BEHAV. 8(5) 543–546, 1978. – Several measures of aggressive behavior were investigated in three ages (40–50, 90–110, and 180–200 days old) and in three strains (Sprague-Dawley, Wistar, and Long-Evans) of rats before and following the administration of mescaline hydrochloride in a shock-elicited aggression situation. The measures included the number of fights, duration of fighting, latency of fighting, number of bites inflicted, and a composite index of pathological aggression. During predrug baseline testing it was found that older rats, regardless of strain, engaged in more frequent fights that were longer in duration and more intense than younger animals. When the animals were tested with mescaline, they engaged in significantly more fights, biting, and pathological aggression than during baseline testing regardless of their age or strain. These results suggest that mescaline-induced pathological aggression in rats is a robust phenomenon.

Footshock Aggression Age Strain Mescaline

WHEN a pair of rats is exposed to repeated presentations of electric footshock they frequently engage in brief episodes of striking each other with their forepaws while upright [1]. Injuries or biting are extremely rare in this situation [2]. However, if they are given mescaline prior to placing them in this situation they will engage in near-lethal fighting behavior. This marked increase in aggressive behavior due to mescaline has been shown to occur reliably on repeated testing with the drug, and is relatively unaffected by previous fighting experience, changing the size of testing enclosure, shock termination, previous familiarity with the drug, or moderate changes in the dosage of the drug [3]. These studies, however, have investigated only one age group (90–110 days old) in one strain (Sprague-Dawley) of rats. Thus it is not known whether these results are readily generalizable to older or younger rats or to rats of different strains.

Since it has been observed that rats in natural settings are more aggressive after physical maturation [4,5] and footshock-induced fighting in rats increases with age [6,7], the occurrence or intensity of mescaline-induced pathological aggression may be age related. Similarly, strain differences in aggressive behavior have been reported for rats exposed to footshock [1], morphine withdrawal [8], as well as in natural settings [4,9]. Thus, the occurrence or intensity of mescaline-induced pathological aggression may also be strain related.

The purpose of this experiment is to determine the generalizability of mescaline-induced pathological aggression in rats by administering the drug to rats of different ages (40–50; 90–110; 180–200 days old) and different strains (Sprague-Dawley, Wistar, and Long-Evans) prior to footshock.

METHOD

Animals

Thirty male Sprague-Dawley, 30 male Wistar, and 30 male Long-Evans rats were obtained from the Simonsen Breeding Laboratories, Gilroy, California, and were used in this experiment. Ten rats in each strain were between 40–50, 90–110 and 180–200 days old at the start of the

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TABLE 1

MEAN BASELINE AND MESCALINE CONDITION SCORES FOR THREE AGE GROUPS AND THREE STRAINS ON MEASURES OF AGGRESSIVE BEHAVIOR*

Age Groups and Strains of Animals	Number of Fights		Number of Bites		Duration of Fighting (sec)		Mean Latency of Fighting (sec)		Index of Pathological Aggression	
	Baseline	Mescaline	Baseline	Mescaline	Baseline	Mescaline	Baseline	Mescaline	Baseline	Mescaline
40–50 days old	4.33	13.47	0.00	0.73	1.45	5.50	3.88	4.82	0.56	1.11
	(2.73)	(5.12)	(0.00)	(0.52)	(0.84)	(2.53)	(0.92)	(1.77)	(0.22)	(0.31)
90–110 days old	17.67	28.53	0.00	14.93	5.61	73.91	2.42	7.79	1.67	2.92
	(4.13)	(6.80)	(0.00)	(6.21)	(1.82)	(43.53)	(0.25)	(1.27)	(0.18)	(0.53)
180–200 days old	23.87	29.73	0.93	15.93	11.71	46.43	3.18	9.69	1.72	2.37
	(6.82)	(7.44)	(0.55)	(6.41)	(3.88)	(37.26)	(0.45)	(2.41)	(0.19)	(0.41)
Sprague-Dawley	17.60	26.93	0.40	17.53	8.00	77.57	2.55	6.96	1.34	2.54
	(6.47)	(8.57)	(0.34)	(7.35)	(3.32)	(46.20)	(0.29)	(1.33)	(0.23)	(0.53)
Long-Evans	13.87	23.67	0.47	3.60	4.94	9.41	3.94	6.73	1.41	1.87
	(4.18)	(4.64)	(0.47)	(2.09)	(1.66)	(2.47)	(0.51)	(1.36)	(0.23)	(0.32)
Wistar	14.40	21.13	0.07	10.47	5.85	38.85	2.08	11.63	1.21	1.98
	(5.05)	(6.58)	(0.07)	(4.99)	(2.29)	(33.94)	(0.20)	(3.51)	(0.26)	(0.51)

*Standard errors are in parentheses

experiment. Each rat was experimentally naive prior to start of the experiment and was housed separately with food and water available at all times.

Apparatus

The chamber used in each experiment consisted of a cylinder with inside dimensions of 30 cm dia. by 30 cm in height. The entire chamber was constructed of clear Plexiglas, which allowed an unobstructed view of its interior. The grid floor of this chamber consisted of 0.63 cm stainless steel rods, spaced 1.27 cm apart (center to center). Electric shock was delivered through the floor grids, operating through a Davis Model 255 grid scrambler. The duration of shock and the interval between shocks were controlled by two Davis Model D 501 time interval generators. The intensity of the shock current was continuously monitored throughout each experimental session by a Tektronics Model 501 oscilloscope. Each aggressive episode and the delivery of shock were recorded concurrently on Davis digital counters, a standard electric cumulative timer, and an Esterline-Angus 20-channel event recorder. The latter device provided a paper tape record of the latency and duration of each fighting episode with respect to the onset of shock.

Procedure

Animals in each strain were weighed at the beginning of the experiment and were paired together on the basis of equal or similar body weight. The difference in weight between animals in a pair never exceeded 5 g. Each pair of rats in each strain was assigned to one of three groups (40–50, 90–110, and 180–200 days old) according to their age to form a total of nine groups of five pairs of rats each. Each pair was initially tested with footshock approximately 20 min after both members received an intraperitoneal injection of 1 cc of distilled water solution per kilogram of body weight. One week later both members of the pair were tested with footshock approximately twenty min following an intraperitoneal injection of 50 mg of mescaline hydrochloride in a distilled water solution per kilogram of body weight.

For aggression testing, a pair of rats was placed in the experimental chamber and received 100 shocks of 2.0 mA for 1.5 sec duration every 30 sec. One observer pressed one of six microswitches to indicate which type of attack occurred and released it when the attack terminated. The criteria for aggressive behavior were identical to those described previously by Sbordone and Garcia [10]. An interobserver reliability coefficient of 0.98 obtained prior to the start of the experiment indicated that each of these categories was easily observable and distinguishable from each other.

Following the completion of each experimental session, this observer recorded his observations in order to provide a complete and detailed record of each experimental session. A second observer initiated the experimental session and recorded any idiosyncratic behaviors or events which occurred during the experimental session. Each testing session lasted approximately 52.5 min.

RESULTS

Differences in aggressive behavior during baseline were examined using a two-way design with Age (40–50 days, 90–110 days, 180–200 days) and Strain (Sprague-Dawley, Long-Evans, Wistar) as between-subjects factors. The dependent variables were the number of fights (total number of fighting episodes regardless of type that occurred during the experimental session), number of bites (the combined total of mild, moderate, and severe biting episodes), duration of fighting (the combined total duration of shoving-lunging, boxing, bite attempt, mild biting, moderate biting, and severe biting episodes), mean latency of fighting (the mean length of time fighting began from the onset of most recent shock), and the index of pathological aggression (shoving-lunging, boxing, attempts to bite, mild biting, moderate biting, and severe biting episodes were assigned numerical weights of 1, 2, 3, 4, 5, and 6, respectively. The frequency of observations for each type of aggressive behavior was multiplied by its respective weight. The sum of all types of fighting was then divided by the total number of observations [10].)

A multivariate analysis of variance (MANOVA) revealed a significant multivariate effect attributable to Age, $F(8,66) = 3.66$, $p<0.0014$. Subsequent univariate analyses revealed significant age group differences in the number of fights, $F(2,36) = 4.36$, $p<0.02$, the duration of fighting, $F(2,36) = 4.35$, $p<0.02$, and in the index of pathological aggression, $F(2,36) = 12.67$, $p<0.0001$. Subsequent Newman-Keuls tests indicated a monotonic increasing trend with a greater number of fights and a longer duration of fighting among successively older age groups of animals. The 180–200 day old rats were significantly greater than the 40–50 day old rats on these two measures (all p's<0.05), and they displayed a nonsignificant trend toward more fights ($p<0.10$) and longer fighting ($p<0.10$) than 90–110 day old rats. In addition, the index of pathological aggression was lower for the younger 40–50 day old animals than it was for the 90–110 day old ($p<0.05$) and 180–200 day old animals ($p<0.05$), but the latter two groups did not differ from one another. The mean baseline and drug level scores for the three ages on all of the aggression measures appear in the upper portion of Table 1.

A two-way univariate analysis of variance with Age and Strain as between-subjects factors was performed on the baseline latency to fight scores of only those animals which engaged in fighting during baseline testing. The results of this analysis revealed a significant effect attributable to Strain, $F(2,24) = 3.64$, $p<0.0417$. Subsequent Newman-Keuls tests indicated that Long-Evans animals showed a longer latency to fight than Sprague-Dawley ($p<0.05$) or Wistar ($p<0.05$) animals, but the latter two strains did not differ from one another ($p<0.05$). The mean baseline and drug level scores for the three strains on the measures of aggressive behavior appear in the lower portion of Table 1.

Differences in aggressive behavior between baseline and drug conditions were examined using a two-way multivariate analysis of variance with Age and Strain as between-subjects factors. The dependent variables were difference scores between baseline and drug treatment for the number of fights, the number of bites, the duration of fighting, and for the index of pathological aggression. The results of this analysis revealed no significant multivariate effects for Age, Strain, or their interaction. However, a significant multivariate effect attributable to the grand mean was observed, $F(4,33) = 4.47$, $p<0.0054$. This result indicates that regardless of Age or Strain, aggressive behaviors following drug administration were significantly greater than baseline levels. Subsequent univariate analyses

TABLE 2

MEAN BASELINE AND MESCALINE CONDITION SCORES FOR MEASURES OF AGGRESSIVE BEHAVIOR*

Measures of Aggressive Behavior	Baseline Condition	Mescaline Condition
Number of Fights	15.29 (3.01)	23.91 (3.85)
Number of Bites	0.31 (0.19)	10.53 (3.09)
Duration of Fighting (sec)	6.26 (1.56)	41.95 (19.15)
Mean Latency of Fighting (sec)	2.96 (0.27)	8.00 (1.13)
Index of Pathological Aggression	1.32 (0.14)	2.13 (0.27)

*Standard errors are in parentheses

performed to determine the relative contribution of each dependent variable to the overall effect [12] revealed that the drug significantly increased the number of fights, $F(1,36) = 4.84$, $p<0.0344$, the number of bites, $F(1,36) = 11.75$, $p<0.0016$, and the index of pathological aggression, $F(1,36) = 15.63$, $p<0.0004$. The mean baseline and drug condition levels appear in Table 2.

A two-way univariate analysis of variance with Age and Strain as between-subjects factors was performed on the baseline-drug latency to fight difference score. This analysis revealed no significant effects for Age or Strain, but found a significant effect attributable to the grand mean, $F(1,24) = 33.39$, $p<0.0001$. This result indicates that regardless of Age or Strain, latency to fight following drug administration was significantly greater than the baseline level. In light of the significant differences previously reported for baseline levels of latency to fight among the three strains, this result indicates that unlike other measures of aggressive behavior the predrug differences were not preserved for latency to fight after drug administration. The mean baseline and drug level scores for this measure appear in Table 2.

DISCUSSION

In the present study several measures of aggressive behavior were evaluated in three ages (40–50, 90–110, and 180–200 days old) and in three strains (Sprague-Dawley, Wistar, and Long-Evans) of rats before and following the administration of mescaline in a shock-elicited aggression situation. The measures included the number of fights, duration of fighting, latency of fighting, number of bites inflicted, and a composite index of pathological fighting intensity. During predrug baseline testing it was found that older rats, regardless of strain, engaged in more frequent fights that were longer in duration and more intense than younger animals. These results are consistent with earlier data reported by Hutchinson *et al.* [6], and Powell and Creer [7]. However, these investigators studied only one strain of rats (Sprague-Dawley), their oldest animals were less than 100 days of age, and they did not examine the intensity of fighting behavior. The present data extend the generalizability of the finding that fighting in a shock-elicited aggression situation increases with age to much older rats and across three different strains.

When the animals were tested with mescaline, they engaged in significantly more fights, biting behavior, and intense fighting than when they were tested with a placebo during baseline. These increases in aggressive behavior due to mescaline were comparable for all ages and strains of rats tested, indicating that initial age and strain differences in these measures of fighting behavior obtained during baseline testing were preserved. The failure, however, to preserve the baseline differences among strains in latency to fight following drug administration suggests that this measure may not be as prepotent in a shock-elicited aggression situation as measures which reflect the amount, duration, and intensity of fighting.

These findings extend the generalizability of mescaline-induced pathological aggression in a shock-elicited aggression situation to rats of widely differing ages and strains. These data, when combined with previous data [3,10] suggest that increased fighting in rats due to mescaline is a robust phenomenon.

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