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Factors influencing the aggressiveness elicited by marihuana in food-deprived rats

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Summary

1. Aggressive behaviour was elicited in rats that had been deprived of food for 20 h daily (starved), by chronic administration of *Cannabis sativa* extract or (−)-Δ^9-*trans*-tetrahydrocannabinol.

2. The influence of intraperitoneal (i.p.) or oral glucose administration, cold environment, acidosis, and corn, and protein-free diets on this aggressiveness was studied.

3. Intraperitoneal injections of glucose (100–1,600 mg/kg) did not alter the aggressiveness induced by marihuana in starved rats; glucose given orally, however, blocked this behaviour.

4. Low temperature (14° C) strongly potentiated the aggressive behaviour induced by marihuana in the starved rats.

5. Lactic acid in doses capable of potentiating thiopental anaesthesia, failed to alter the marihuana-aggressiveness of starved rats or to facilitate this effect of marihuana in rats fed *ad libitum*. The same negative results were obtained with ammonium chloride.

6. In rats fed *ad libitum* with protein-free or corn diets, marihuana administered chronically did not elicit aggressive behaviour. However, aggressiveness appeared when rats were fed for only 2 h daily on those diets.

7. The results suggest that the stress of hunger (and not hypoglycaemia, acidosis or lack of specific nutrients due to starvation) is the factor that facilitates the development of aggressive behaviour by chronic administration of marihuana.

Introduction

It has been reported that chronic administration of *Cannabis sativa* extracts elicits striking fighting behaviour in rats deprived of food for 20–22 h daily (Carlini & Masur, 1969; Orsingher & Fulginiti, 1970). Further experiments carried out to determine the specificity of the effect seen with marihuana have shown that amphetamine, amylobarbitone, mescaline, LSD-25 and caffeine do not induce this behaviour alteration; (−)-Δ^9-*trans*-tetrahydrocannabinol (Δ^9-THC), however, does (Carlini & Masur, 1970). On the other hand, the aggressive behaviour displayed by the rats is only seen under the double treatment, marihuana plus food deprivation. Thus, rats fed *ad libitum* do not show it after 30–40 injections of marihuana; the aggressiveness also does not appear when food-deprived

rats are chronically treated with control solution. Therefore, it seems clear that food deprivation is of paramount importance for the appearance of this effect of cannabis.

The present work was designed to analyse this point further. It was tentatively suggested that one of the following factors, hypoglycaemia, acidosis or lack of some nutritional element, could be the factor which facilitates the induction of aggressiveness in rats by marihuana. The experiments described below were carried out to test these possibilities.

Methods

Three hundred and seventy-eight male and female Wistar rats, ages ranging from 3 to 4 months, were housed in pairs in wire cages measuring $16 \times 30 \times 18$ cm. For each experimental condition 3 to 7 pairs of rats were used and the groups were matched for age and sex within each experiment. After intraperitoneal injection of the marihuana extract or the control solution the animals were observed for aggressive behaviour during 2 or 3 hours. At the end of the observation period the rats were allowed 2 h of free access to food; therefore the animals were food-deprived 19–22 h daily and such animals will be referred to as either food-deprived or starved rats. In all experiments the injections of marihuana and control solution started on the first day of restricted access to food. Aggressive behaviour was timed with a stopwatch and corresponded to the time in seconds both rats of a pair assumed a stereotyped fighting position standing on their hind-legs ('boxer position') trying to bite each other. In general, aggressiveness appeared within 30–40 min after the injections and persisted for 2 to 4 hours. During this time the animals showed great irritability, vocalization, reacted violently to noise or puffs of air and vigorously attacked their cagemates. However, as stated above, only the actual fighting ('boxer position') was timed. In one experiment shock-induced aggressive behaviour was also assessed during a 10 min period beginning 50 min after the injections. For further details of the methods see Carlini & Masur (1969).

The marihuana extracts and the control solution were prepared according to Carlini & Kramer (1965). Briefly, the plant material was extracted for 12 h with petroleum ether in a reflux condenser; after getting rid of the solvent the resin obtained was suspended in alcohol and kept in darkness at 4° C. To prepare the extract the alcohol was evaporated and the residue suspended in saline with Tween-80 (3 drops of Tween-80 per 10 ml of saline). The control solution was composed of saline plus Tween-80 in the same proportions. Flowering tops of *Cannabis sativa* from Mato Grosso State (extracts Q_4 and Q_5) and Brasilia city (extract B) were employed; our thanks are due to Drs. Orlando Rozante and Walmores V. Barbosa for the supply of these materials. Pure (−)-Δ^9-*trans*-tetrahydrocannabinol was used in one experiment; we are grateful to Drs. F. Korte and D. Bieniek for the gift of this compound. The potency of the three extracts and of pure Δ^9-THC as assayed by the corneal areflexia method in rabbits (Gayer test) according to Santos, Sampaio, Fernandes & Garlini (1966) was, respectively, $0{\cdot}40 \pm 0{\cdot}12$, $0{\cdot}34 \pm 0{\cdot}09$, $0{\cdot}42 \pm 0{\cdot}19$ and $0{\cdot}10 \pm 0{\cdot}09$. Unless otherwise stated the animals were fed with a commercially available food pellet diet (*normal* diet) prepared from peanut flour, soybean, meat, bone and fish with the following minimum

per cent composition: protein 21·8, fat 3·5, fibre 5·5, minerals 7·5, calcium 1·7 and phosphorus 0·8. One hundred and fifty mg of mineral mixture, 5,000 IU of vitamin A and 1,000 IU of vitamin D_3 were added to each kilogramme of diet.

The *balanced* diet used in some experiments had the following per cent composition: casein 27, corn starch 47, soybean oil 8, sucrose 10, fibre 3·0, mineral mixture 4·0 and vitamin mixture 1·0. The *protein-free* diet was composed of 74% corn starch, 8% soybean oil, 10% sucrose, 4% mineral mixture, 3% fibre and 1% vitamin mixture. We are grateful to Dr. Sergio M. Zucas, from University of São Paulo, for the generous gift of the diets.

The following experiments were performed.

Influence of intra-peritoneal (i.p.) injections of glucose on marihuana aggressiveness (see Table 1)

Twenty-three pairs of food-deprived rats (3 months old) were treated daily with 10 mg/kg of extract Q_5 for 15 days. The experiments were carried out at room temperature, which varied from 20° to 26° C. Fierce aggressiveness beginning after the 11th day appeared in 14 pairs, which were used thereafter. After the 13th marihuana injection, fighting behaviour was scored in seconds during 30 min after it began. Then glucose (100–800 mg/kg) was injected i.p. and aggressiveness was scored again for 30 minutes. Three more injections at 30 min intervals followed: one of control solution, one of glucose, and another of control solution, respectively, during which aggressiveness continued to be measured. On the 15th day the same procedure was repeated; however, the order of the injections was control solution, glucose, control solution and glucose. On the following day (16th), glucose (800 mg/kg) and control solution were injected 5 min before the marihuana administration.

Influence of oral glucose on marihuana aggressiveness (see Table 2)

Five pairs of 3 month old female rats starved 22 h daily were injected daily with cannabis extract Q_5 (10 mg/kg) for 25 days; the temperature varied from 19° to 24° C. After 13 days, aggressiveness, scored for 2 h, was evident in 4 pairs. In the following two days (14th and 15th) the rats were allowed to drink a 10% glucose solution *ad libitum*; from the 16th to the 25th days tap water was given again.

Influence of temperature on marihuana aggressiveness (see Table 3)

Twenty pairs of male rats 4 months old were deprived of food for 22 hours. During this time, half the animals were housed in a room with temperature maintained at $27 \pm 1°$ C; the other 10 pairs were left in a cold room ($14 \pm 1°$ C). Half the rats in each room were then injected with cannabis extract B (10 mg/kg) and the remaining animals with control solution. Aggressiveness was scored during the next 3 h; food was then given for a 2 h period. On the following day the same procedure was repeated. From the third to the 20th day the treatment continued only for the animals living at 27° C.

Influence of acidifying agents on marihuana aggressiveness

Preliminary experiments with 40 rats have shown that the largest single doses of ammonium chloride and lactic acid tolerated by the animals without depression

were 200 and 20 mg/kg, respectively. Acute and chronic experiments were then performed with 3 month old rats ; the temperature ranged from 20° to 26° C.

Acute experiments (see Table 4)

Thirty pairs of male rats fed *ad libitum* were used. Five pairs received 4 doses of ammonium chloride (100 mg/kg) at 6 h intervals ; 30 min after the last injection, cannabis extract Q_4 (10 mg/kg) was injected and spontaneous and shock-induced aggressiveness were scored for 3 hours. Two other pairs of rats fed *ad libitum* received similar treatment, but ammonium chloride was given in 3 doses of 200 mg/kg at 4 h intervals. Pretreatment with lactic acid was as follows: two pairs of rats fed *ad libitum* received one dose of 10 mg/kg and another two pairs 20 mg/kg ; 5 min late marihuana was injected. Finally, 5 pairs were injected 3 times with 10 mg/kg of lactic acid, at 3 h intervals, and 5 min after the last injection 10 mg/kg of marihuana was given.

For all groups treated with the acidifying agents plus marihuana, similar groups of rats received the same number of injections of saline plus marihuana. In one control experiment the influence of lactic acid (20 mg/kg) on thiopental anaesthesia was assessed in 5 rats.

Chronic experiments (see Table 5)

Five groups of 7 pairs of 4 month old female rats starved 20 h daily were used. Three groups were injected with saline and received 5 min later, respectively, control solution, cannabis extract Q_4 (10 mg/kg) and Δ^9-THC (2·5 mg/kg). The remaining 2 groups were pretreated with lactic acid (10 mg/kg) 5 min before the injections of extract Q_4 (10 mg/kg) and of Δ^9-THC (2·5 mg/kg) respectively. After the marihuana injections aggressiveness was scored during the following 2 hours. The treatment continued for 28 days.

Influence of corn diet on marihuana aggressiveness (see Table 6)

Six pairs of 4 month old male rats were used. Half the animals received corn for 2 h daily as their only diet ; the other 3 pairs were fed for the same time with a normal diet of pellets. Aggressiveness was measured for 2 h daily beginning immediately after the injection of extract B (10 mg/kg). The experiment continued for 7 days during which the temperature ranged from 23° to 29° C.

Influence of protein-free, balanced and corn diets on marihuana aggressiveness (see Table 7)

Nine groups of 5 pairs of 3 month old male rats were used. Three groups were maintained in a cold room with a temperature of 16° C ; each of these groups received, respectively, corn, protein-free or balanced diets *ad libitum*. The other six groups were kept at room temperature which varied from 19° to 25° C ; half of these animals received the diets above *ad libitum* and the other half only for 2 hours. Cannabis extract Q_5 (10 mg/kg) was injected daily for 29 days ; aggressiveness was measured for 2 h after the injections.

TABLE 1. *Influence of I.P. injections of glucose on the fighting behaviour elicited in starved rats by* 10 *mg/kg of cannabis extract* Q_5. *Glucose was injected on the* 13*th and* 15*th days after beginning of daily treatment with cannabis*

Day	Number of animals	Average fighting ($s \pm$ S.E.) during consecutive periods of 30 min following injections of: No drug	Glucose (mg/kg) 100	200	400	800	Control solution (1·0 ml/kg)	Glucose (mg/kg) 400	800	Control solution (1·0 ml/kg)
13	1	360*	900	—	—	—	—	—	—	—
	1	420	—	430	—	—	135	—	—	—
	8	1,367±244	—	—	1,245±253	—	1,396±222	1,381±105	—	1,362±105
	4	1,650±150	—	—	—	1,616±109	1,476±199	—	1,386±223	1,299±266

Day	Number of animals	No drug	Control solution (1·0 ml/kg)	Glucose (mg/kg) 100	200	400	800	Control solution (1·0 ml/kg)	400	Glucose (mg/kg) 800
15	1	489	600	510	—	—	—	—	—	—
	1	760	75	—	0	—	—	—	—	—
	8	1,370±232	1,423±199	—	—	1,302±277	—	1,562±241	1,259±260	—
	4	1,527±107	1,583±178	—	—	—	1,547±206	1,467±252	—	1,383±262

*Lack of S.E. means that just one pair fought. Same in the following tables.

Results

Marihuana-aggressiveness and glucose

As seen in Table 1, doses of glucose up to 1·6 g/kg injected after the appearance of marihuana-induced aggressiveness were not able to counteract it. Furthermore, 800 mg/kg of glucose injected 5 min before the administration of the extract was also ineffective. A different result was obtained, however, when the rats were allowed to drink a 10% glucose solution. Thus, as shown in Table 2, after the rats were given free access to glucose for 24 and 48 h, injection of marihuana did not elicit the aggressive behaviour as it did on the two previous days; the rats drank an average of 41 ml of solution in each 24 h period. Repeating the cannabis injections for 10 more days, without further oral glucose, did not restore the aggressive behaviour.

Marihuana-aggressiveness and temperature

The food-deprived rats submitted to 14° C for 22 h showed fierce aggressiveness beginning with the first injection of marihuana (Table 3). The same result was

TABLE 2. *Influence of oral glucose administration on the fighting behaviour elicited in starved rats by 10 mg/kg of extract Q_5*

Average fighting ($s \pm$ S.E.) during 2 h after injection number and ingestion of					
12 water	13 water	14 glucose	15 glucose	20 water	25 water
1,197±412	1,077±211	0	0	0	0

TABLE 3. *Influence of temperature on the fighting behaviour elicited in starved rats by 10 mg/kg of cannabis extract B*

Drug	Temperature (°C)	Average fighting ($s \pm$ S.E.) during 3 h after injection number 1	2	15	20
Cannabis Extract	14	4,600±1,520	5,041±1,981	–	–
	27	0	0	285±182	217±79
Control Solution	14	0	0	–	–
	27	0	0	0	0

TABLE 4. *Lack of influence of ammonium chloride and lactic acid injections on the aggressive behaviour elicited in rats, fed* ad libitum, *by 10 mg/kg of cannabis extract Q_4*

	Pre-treatment				Duration of aggressive behaviour (*s*) after marihuana	
Drug	Number of rats	Dose (mg/kg)	No. of injections	Time interval between injections (h)	Shock-induced	Spontaneous
NH_4Cl	5	100	4	6	0	0
Control solution	5	1·0 ml/kg	4	6	0	0
NH_4Cl	2	200	3	4	54; 2	0
Control solution	2	1·0 ml/kg	3	4	74; 1	0
Control solution	2	1·0 ml/kg	1	–	0	0
Lactic acid	2	10	1	–	0	0
Lactic acid	2	20	1	–	0	0
Control solution	5	1·0 ml/kg	3	2	0	0
Lactic acid	5	10	3	2	0	0

obtained on the second day when most rats died during the fighting. In contrast, starved animals maintained at 27° C and receiving the same sample of cannabis did not show signs of aggressiveness until the 15th injection (Table 3).

Marihuana-aggressiveness and acidifying agents

Table 4 shows that neither lactic acid nor ammonium chloride were able to potentiate the aggressiveness-inducing properties of marihuana extract and Δ^9-THC. Thus, rats fed *ad libitum* and pretreated with several doses of the acidifying agents did not show spontaneous or shock-induced aggressive behaviour after the first dose of marihuana. The results with chronic treatment were also negative ; thus, as seen in Table 5, aggressiveness produced by Δ^9-THC or cannabis extract was not affected by pretreatment with lactic acid during 28 days.

On the other hand, lactic acid (20 mg/kg) strongly potentiated the effects of sodium thiopental (50 mg/kg) ; thus, 5 control rats slept 180 ± 19 min (average $\pm$ S.D.) under thiopental, whereas 2 animals pretreated with the acid died and the other 3 slept 375 ± 65 min after receiving the barbiturate.

Marihuana-aggressiveness and diet

Rats fed exclusively on corn diet for 2 h daily showed an aggressive behaviour comparable to that of animals receiving normal diet for the same period of time (Table 6). After the 5th injection, however, aggressiveness decreased in the corn-treated animals, probably because they were weaker, weighing less than animals on a 2 h normal diet. Table 7 shows that feeding rats *ad libitum* with corn, protein-free or balanced diets, either at room temperature (first 3 rows of Table 7) or 16° C (4th to 6th rows) did not increase the aggressiveness-inducing property of marihuana. However, when the 3 diets were given only for 2 h, aggressiveness appeared as usual (last three rows) although the duration of fighting was greater in the protein-free diet group.

TABLE 5. *Lack of influence of* 10 *mg/kg of lactic acid on the aggressive behaviour elicited in starved rats by* 10 *mg/kg of cannabis extract* Q_4 *and* 2·5 *mg/kg of* Δ^9*-THC*

Pre-treatment Drug	Treatment Drug	Dose (mg/kg)	Average fighting ($s \pm$S.E.) during 2 h after marihuana injection number						
			1	5	10	15	20	25	28
Saline	Control soln.	1·0 ml/kg	0	0	0	0	0	0	0
Saline	Cannabis	10	0	45	0	460±101	0	232±39	239± 85
Saline	Δ^9-THC	2·5	0	0	0	0	348±182	21	201±102
Lactic acid	Cannabis	10	123	0	15	679±199	93	151±39	103± 34
Lactic acid	Δ^9-THC	2·5	0	0	0	0	0	43	259±181

TABLE 6. *Influence of normal and corn diets on the aggressive behaviour elicited in rats by* 10 *mg/kg of cannabis extract B*

Diet	Average fighting ($s \pm$S.E.) during 3 h after marihuana injection number						
	1	2	3	4	5	6	7
Normal	0	0	2,608±1,037	2,921±1,112	2,608±1,104	2,755±985	1,201±1,087
Corn	0	118	2,220±1,002	2,224± 892	1,013± 801*	317±218*	400±114*

* Statistically significant difference ($P \leq 0{\cdot}05$; Mann-Whitney U test).

TABLE 7. *Influence of corn, protein-free and balanced diets on aggressive behaviour elicited in satiated or starved rats treated with* 10 *mg/kg of cannabis extract* Q_5 *and maintained at room temperature or in a cold room*

Diet	Daily feeding	Temperature °C	Average fighting ($s \pm$ S.E.) during 2 h after marihuana injection number 1	5	10	15	20	25	29
Balanced	*ad libitum*	19–25·5	0	1	15	0	0	0	0
Protein-free	,, ,,	,, ,,	0	13	0	0	25	0	8
Corn	,, ,,	,, ,,	0	7	28	0	0	0	0
Balanced	*ad libitum*	16	9	0	0	4	0	20	7
Protein-free	,, ,,	,,	55	0	0	662±294*	0	82	49
Corn	,, ,,	,,	13	0	15	27	0	240±81*	61±30*
Balanced	2 h	19–25·5	0	0	2	98±51	206±98	723±217	201±64
Protein-free	,,	,, ,,	0	0	0	0	510±108*	1,244±508*	742±118*
Corn	,,	,, ,,	0	0	0	0	222±74	517±181	308±171

*Statistically significant difference from group fed with balanced diet ($P \leq 0{\cdot}05$; Mann-Whitney U test)

Discussion

The results described here confirm previous reports on the aggressive behaviour elicited in food-deprived rats by chronic administration of marihuana (Carlini & Masur, 1969, 1970; Orsingher & Fulginiti, 1970). The present experiments were carried out with 3 extracts of *Cannabis sativa* and one sample of pure Δ^9-THC. The extracts possessed approximately the same potency, which was equal to one quarter of that of Δ^9-THC, as measured by the Gayer test. According to Carlini, Santos, Claussen, Bieniek & Korte (1970) this test gives a reliable measure of Δ^9-THC content in cannabis extracts. Therefore, as the extracts were used in doses 4 times greater than that of Δ^9-THC, the rats received approximately the same amount of Δ^9-THC in all experiments. The rats used were of either sex, and from 3 to 4 months of age. However, the influence of the several conditions on marihuana-aggressiveness was studied with the rats as their own controls or with the use of appropriate control groups matched for sex and age. Furthermore, Carlini & Masur (1969) have shown that marihuana-induced aggressiveness does not depend on the sex and age of rats older than 2 months. Finally, in several experiments the temperature was not kept constant (range 19 to 29° C); however, in this and in our previous work (Carlini & Masur, 1969, 1970), it was shown with appropriate control groups of rats that changes in temperature alone did not induce observable changes in behaviour.

It has been reported that food deprivation leads rats to increased excitability and aggressiveness (Davis, 1933; Moyer, 1968). In our conditions, however, aggressiveness did not appear in 288 chronically starved rats used as controls in several other experiments. These animals showed at most excitability, but vicious bitings and stereotyped fighting ('boxer position') lasting for minutes to hours, as observed in the cannabis-treated animals, have never been observed. On the other hand, as shown here and previously by Carlini & Masur (1969, 1970), marihuana does not induce aggressiveness unless the rats are starved.

Of the several conditions studied here only two, namely oral glucose and decrease of temperature, affected the aggressive behaviour induced by marihuana in starved rats. Low temperature clearly potentiated the aggressiveness. As seen in Table 3, marihuana injected in starved rats maintained at 14° C induced fierce aggressiveness in the first 2 days; at 27° C, however, it took 15 injections to achieve aggressive behaviour. This influence of temperature has been observed before (Carlini & Masur, 1969). After drinking about 40 ml of glucose solution in 24 h, which corresponded to 4 g, the animals which were previously aggressive no longer fought under marihuana (Table 2). This effect was probably not brought about simply by an elevation of blood glucose, because if that was the case then intraperitoneal administration would have given the same result. However, 800–1,600 mg/kg of glucose injected at the peak of aggressiveness or 5 min before marihuana administration did not diminish aggressiveness (Table 1). This amount of glucose corresponds roughly to 10 to 20 times the total amount of glucose in the blood of rats. On the other hand, the animals drank at the most 1·3 ml of solution in the last hour before the cannabis injection, which corresponds to about 600 mg/kg of glucose ingested, a value within the range of the intraperitoneal administration. Therefore, the inhibition of aggressive behaviour by oral glucose should not be attributed to an increase of glucose levels in blood.

Eventual changes of pH due to acidosis that may occur in food deprivation, are probably not the potentiating factor. It is known that pH changes influence the penetration of weak acids such as barbiturate into brain (Brodie & Hogben, 1957) and Δ^9-THC has a phenolic moiety in its dibenzopyran nucleus. Although no information is available concerning its dissociation properties, Δ^9-THC and other marihuana compounds might be inducing aggressiveness in starved rats through increased penetration caused by the acidosis. The results obtained, however, do not support this hypothesis. Lactic acid which clearly potentiated thiopental, did not cause cannabis to elicit aggressiveness in rats fed *ad libitum* or to increase fighting in starved rats ; the same negative results were also obtained with ammonium chloride (Tables 4 and 5).

It is also improbable that lack of a nutritional element could be the facilitating factor. Lack of tryptophan leads to a decrease in 5-hydroxytryptamine in brain (Culley, Saunders, Mertz & Jolly, 1963) ; an inhibitory function on central nervous system has been attributed to serotonin (Brodie & Reid, 1968 ; Kostowski, Giacalone, Garattini & Valzelli, 1969) and a correlation between aggression and low serotonin content in brain has been reported (Garattini, Giacalone & Valzelli, 1967 ; Lycke, Modigh & Roos, 1969). However, rats fed *ad libitum* exclusively on a corn diet which contains little tryptophan (Karlson, 1965) did not show marihuana-aggressiveness at room temperature (Table 7) ; even at 16° C there was little aggressiveness (Table 7). On the other hand, rats fed 2 h daily with corn, in two experiments at room temperature (Tables 6 and 7), showed a marihuana-aggressiveness comparable to that observed in animals fed for 2 h with normal and balanced diets.

Decrease of protein in starved animals also does not seem to be the important factor. Δ^9-THC binds to about 80–95% in plasma protein (Wahlquist, Nilsson, Sandberg, Agurell & Granstrand, 1970) ; thus, in hypoproteinemic animals marihuana compounds may reach the brain more easily. However, animals maintained at room temperature or at 16° C and fed *ad libitum* exclusively on a protein-free diet did not develop aggressive behaviour even after 29 marihuana injections (Table 7 ; 2nd and 5th rows). Typical aggressiveness appeared only when the rats were maintained on protein-free diet for 2 h daily (Table 7 ; 8th row).

It is interesting to analyse the failure of marihuana to induce aggressive behaviour in rats on protein-free and corn diets *ad libitum*. These rats ate a great deal but lost weight as compared with animals which fed for 2 h on normal or balanced diets ; thus, these animals lost 18·1 and 17·2% of their initial weight, respectively, which did not differ significantly from the 16·4 and 20·1% losses in groups on 2 h normal and balanced diets. This indicates that they were also undernourished. However, aggressiveness appeared only in rats receiving the 2 h diets. This suggests that undernourishment *per se* is not the facilitating factor for the induction of aggressive behaviour by marihuana. On the other hand, when glucose was given by injection aggressiveness remained, whereas when rats were allowed to drink glucose aggressive behaviour was prevented. It seems therefore that if rats are allowed to eat at will, aggression as a result of injections of marihuana does not appear, even when deficient diets are furnished. These data suggest that hunger stress rather than undernourishment, is important for facilitating marihuana-induced aggressive behaviour in the starved rat. In support of this conclusion are the data

that in rats submitted at the same time to two stressful situations, food deprivation and cold, aggressiveness was more intensely and more easily elicited by marihuana (Table 3). The possibility that environmental stresses may potentiate cannabis effects has also been suggested for human beings (Talbott & Teague, 1969).

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