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Post-Swim Grooming in Mice Inhibited by Dopamine Receptor Antagonists and by Cannabinoids

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CHESHER, G. B. AND D. M. JACKSON. *Post-swim grooming in mice inhibited by dopamine receptor antagonists and by cannabinoids*. PHARMAC. BIOCHEM. BEHAV. 13(3) 479–481, 1980.—After a period of swimming, mice engaged in vigorous grooming activity. This behaviour was inhibited in a dose dependent manner by dopamine receptor antagonists and by the cannabinoids, Δ^9-tetrahydrocannabinol and cannabinol. Cannabidiol was inactive. It is suggested that the post-swim grooming behaviour involves a dopaminergic mechanism. The mechanism of action of the cannabinoids on this behaviour is unknown.

Grooming Dopamine receptor antagonists Δ^9-Tetrahydrocannabinol Cannabinol Cannabidiol

DURING studies of swim-stress induced analgesia in mice, it was noted that the animals engaged in intensive grooming activity after they had been removed from the water. Animals which had been pretreated with Δ^9-tetrahydrocannabinol (THC) were observed to exhibit a striking reduction in their post-swim grooming behaviour.

In this communication, we present evidence that grooming behaviour induced by swimming is reduced in a dose dependent manner by the cannabinoids, tetrahydrocannabinol (THC) and cannabinol (CBN) and by dopamine (DA) receptor antagonists.

METHOD

QS strain female mice (20–30 g) were kept at 22 ± 1° with free access to food and water up to the time of the experiment. After appropriate drug premedication, groups of six mice were placed in a water bath (39×20×15 cm) containing water at 32° to a depth of 10 cm. After a swimming time of 3 min, the mice were removed, and after excess water had been allowed to drain off, each mouse was placed into a clear perspex observation chamber (95×65×65 mm). By means of an electronic timing device which emitted a tone each 10 sec, one mouse was assessed at each tone signal. In this manner, using groups of six mice, each mouse was assessed for presence or absence of grooming behaviour once per minute for 30 min. A score of 1 was given if at the time of the assessment the animal was engaged in grooming activity and 0 if not grooming. The maximum possible grooming score for each was therefore 30.

The drugs used were haloperidol (Searle), spiroperidol (Janssen Pharmaceutical), chlorpromazine hydrochloride (Smith, Kline and French), THC, CBN, and cannabidiol (CBD) (National Institute of Drug Abuse, U.S.A.). Haloperidol and spiroperidol were dissolved in glacial acetic acid and diluted with water (final pH 3.5–4.0); chlorpromazine hydrochloride was dissolved in water, and all were administered IP 1 hr before swimming the mice. The cannabinoids were suspended in a mixture containing 1% Tween-80, 10% propylene glycol in saline (0.9%) and were administered IP 30 min before swimming. Control animals for each group were dosed with the appropriate vehicle given in equivalent volume at the same time before swimming the test mice.

At least three doses of each drug were used to construct dose-response curves. These were for spiroperidol (0.2, 0.4, 0.8 and 1.2 μmoles/kg (79 to 475 μg/kg)), haloperidol (0.133, 0.266, 0.532, 0.80 and 1.332 μmoles/kg (50 to 500 μg/kg)), chlorpromazine (6.25, 12.5, and 25.0 μmoles/kg (2.2 to 8.8 mg/kg)), tetrahydrocannabinol (0.52, 1.03, 2.39, 4.77, 9.54 and 19.08 μmoles/kg (163 to 6000 μg/kg)), cannabinol (16.1, 32.21, 64.43 and 128.86 μmoles/kg (5.0 to 40.0 mg/kg)), and cannabidiol (31.8, 63.6, 127.2 and 254.4 μmoles/kg (10 to 80 mg/kg)). The total grooming score for each mouse was expressed as a percentage of the mean grooming score for the control group. The mean of the percent grooming score for each dosage group was used for the calculation of results by probit analysis [3].

RESULTS

The results are detailed in Table 1 and summarized in Table 2. Haloperidol, spiroperidol, chlorpromazine, THC and CBN produced a dose dependent depression of the swim-induced grooming behaviour in mice. Tetrahydrocannabinol was approximately equiactive with chlorpromazine and was about seven times more potent than CBN. CBD was relatively inactive in doses up to 254 μM/kg, although at the highest dose level an approximately 30% inhibition of grooming was observed.

TABLE 1

THE EFFECT OF PRETREATMENTS WITH VARIOUS DRUGS ON POST-SWIM GROOMING BEHAVIOUR IN MICE. THE DATA ARE EXPRESSED AS A PERCENTAGE OF THE APPROPRIATE CONTROL ± SEM AND THE ABSOLUTE NUMBER OF GROOMING INCIDENCES FOR EACH CONTROL IS GIVEN IN BRACKETS. "n" IS THE NUMBER OF ANIMALS USED FOR EACH PRETREATMENT

Drug	Dose (μmoles/kg)	Percent of control response	n
Spiroperidol	0	100 (24 ± 1.0)	12
	0.2	69 ± 11	6
	0.4	63 ± 10	10
	0.8	39 ± 10	10
	1.2	8 ± 2	10
Haloperidol	0	100 (23.4 ± 1.05)	16
	0.133	89 ± 5	12
	0.266	60 ± 7	12
	0.532	62 ± 5	8
	0.80	45 ± 5	8
	1.332	22 ± 3	13
Chlorpromazine	0	100 (24.1 ± 1.0)	9
	6.25	63 ± 7	8
	12.50	33 ± 12	8
	25.0	1 ± 0	5
Tetrahydrocannabinol	0	100 (23.0 ± 0.5)	23
	0.52	97 ± 5	10
	1.03	89 ± 7	10
	2.39	77 ± 10	10
	4.77	71 ± 7	10
	9.54	41 ± 8	10
	19.08	18 ± 5	10
Cannabinol	0	100 (22.5 ± 2.4)	6
	16.11	92 ± 16	6
	32.21	60 ± 13	6
	64.43	41 ± 6	6
	128.86	10 ± 4	6
Cannabidiol	0	100 (21.8 ± 1.5)	12
	31.8	87 ± 10	7
	63.6	98 ± 9	6
	127.2	102 ± 9	8
	254.4	69.5 ± 16.7	6

TABLE 2

THE ID_{50} (μmoles/kg ± SEM) VALUES FOR VARIOUS DRUGS IN INHIBITING POST-SWIM GROOMING BEHAVIOUR IN MICE

Drug	ID_{50}*	SEM	n*
Spiroperidol	0.42	0.10	48
Haloperidol	0.59	0.15	69
Chlorpromazine	8.18	1.79	30
Tetrahydrocannabinol	6.90	0.64	83
Cannabinol	47.07	11.36	30
Cannabidiol	>254	—	39

*ID_{50} is defined as the dose of drug required to inhibit the grooming response of mice to 50% of vehicle treated animals. n is the total number of animals used to assess the ID_{50}.

DISCUSSION

The results suggest that the grooming behaviour induced in mice by swimming involves a dopaminergic mechanism since it was inhibited in a dose-dependent manner by three DA receptor antagonists. Furthermore, the rank order of potency of the three antagonists (i.e. spiroperidol>haloperidol>chlorpromazine) was the same as that obtained in many other DA mediated behaviours and actions, [5]. However, it should be noted that DA receptor blockade might be expected to interfere with any behaviour requiring initiation of voluntary movements or co-ordination of complex motor acts. The inhibition in this context might be due to generalised suppression of responding. Nevertheless, the potency of the neuroleptics obtained in the present experiment does correspond with the efficacy in blocking other DA mediated behaviours [5]. Moreover, other drugs such as α-methyl tyrosine in sedative doses as high as 400 mg/kg did not block the grooming behaviour (Chesher and Jackson, unpublished data). Rohte [7] reported that chlorpromazine and haloperidol blocked charcoal-induced grooming in mice at doses of 8 and 1 mg/kg respectively. The ID50 values in the present experiments were somewhat lower than these data (3.12 mg/kg and 157 μg/kg respectively).

The cannabinoids, THC and CBN also inhibited this behaviour, and one can only speculate as to the mechanism involved; however, an interaction of THC with a central dopaminergic system has been described earlier by us [4]. THC was about seven times more potent than CBN and this relative potency is one that has been reported for many pharmacological parameters; for example, the antinociceptive activity in mice, using the hot plate method [2] and for the attenuation of quasi-morphine withdrawal syndrome in rats (Chesher and Jackson, unpublished data). Furthermore, a similar potency ratio for these two cannabinoids has been reported for their psychoactivity in man [6]. It seems unlikely that the effects observed here with THC and CBN are due to a non-specific depression because the doses chosen (especially for THC) were low with little effect on locomotor activity [1].

We are presently examining the mechanism of action of the cannabinoids on this parameter and also the possible involvement of neurotransmitters other than DA.

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