may have come from the stores in the muscle itself or from the nerve fibres but the experiments do not allow a firm conclusion to be drawn about the origin of the prostaglandin E.

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Cannabis-induced vocalization in the rat

A disadvantage of previous methods of assaying the potency of cannabis preparations (Dixon, 1899; Gayer, 1928; Valle, 1967a,b) is that they cannot be used for determining effect of cannabis in rats. One possible approach is to use the degree of ataxia or catalepsy induced by the drug, another is to use vocalization as reported by Carlini & Kramer (1965). They found that, under the influence of cannabis, rats vocalize when they are touched.

We have set out to find if vocalization is a relevant indicator of cannabis effect. As reported by Boyd, Hutchington & others (1963) we also found that even low doses of cannabis produce a decrease in fixed ratio responding for food in rats. We have therefore compared the minimal doses necessary to affect vocalization with bar-pressing behaviour for food in a fixed ratio (FR) program.

Adult male albino rats of the Sprague-Dawley strain, weighing 300–350 g, 10 animals to each dose, were tested with cannabis extract (75% tetrahydrocannabinol, 7% cannabinol, 11% cannabidiol) or synthetic Δ^9- and Δ^8-tetrahydrocannabinol (THC) intraperitonally or orally, to assess the drugs' ability to dispose the animals to vocalization. The drugs were dissolved either in propylene glycol or olive oil. In an inhalation experiment, raw material (3·2% tetrahydrocannabinol, 1·2% cannabinol, 5·1% cannabidiol), as smoke, was tested, the rats being confined in a closed acrylic cage (22 × 15 × 15 cm) for 10–15 min after it had been filled with pure cannabis- or tobacco-smoke. The amount used varied between 0·60–0·80 g/rat.

Animals were tested in their individual cages. After the administration of the drugs, the rats were gently pressed with thumb and forefinger by the experimenter 2–4 times bilaterally behind their forelimbs on the ventral aspect of the frontal costal region every 5 min, to find the onset and duration of the vocalization behaviour and to see if habituation occurred.

In the fixed ratio experiment, six animals, trained at a FR30 schedule of reinforcement performing in daily sessions of 15 min, were used. The apparatus was standard operant conditioning equipment.

Vocalization could be produced in animals given: extract, in propylene glycol, in doses of 5 mg/kg, i.p. or more (one of ten animals did not vocalize at 10 mg/kg); extract, in propylene glycol or olive oil, orally in doses of 50 mg/kg or more; raw

material, inhaled as smoke; Δ^9-THC, in propylene glycol, in doses of 1·5 mg/kg, i.p. or more (two of ten animals did not vocalize at 1·5 mg/kg); Δ^8-THC, in propylene glycol, in doses of 2 mg/kg, i.p. or more (one of ten animals did not vocalize at 5 mg/kg).

Vocalization did not occur when the animals were given: extract in olive oil, in doses of 70 mg/kg, i.p., or less, or in doses of 35 mg/kg, orally, or less (four out of ten animals vocalized at 25–35 mg); solvents only, given i.p. or orally; tobacco, inhaled as smoke; Δ^9-THC, in propylene glycol, 0·80 mg/kg, i.p.

The vocalization behaviour generally appeared within 15 min of the drug being given, except after the oral administration of extract in oil, where the onset appeared after 1 h. In some animals it occurred after 5 min. No habituation to touching was noted even after 5–6 h.

To see if there was any sensitization to pressing, one experimental and one control group (n = 20/group) were given tetrahydrocannabinols daily for six days and then tested with solvent only. No vocalization occurred at the day of testing. The lack of effect with olive oil as solvent is probably because the drug absorption was prolonged. In a comparison of the minimal doses that affected vocalization with those affecting fixed-ratio behaviour it was found that when vocalization was present there was also a dose-dependent reduction in responding. Δ^9- and Δ^8-THC, 1·5–5·0 and 2·0–10·0 mg/kg, produced decrements in bar-pressing ranging from 20–100% and 8–100% respectively.

Not on every occasion did a usually effective dose of the drugs affect the operant-behaviour but in these cases there were neither vocalization, nor any other overt behavioral sign. This might be the result of faulty administration of drug or of individual variations of the animals in reacting to the drugs. We did observe that every time the behaviour was affected the rats always vocalized before and after the test. We conclude that vocalization may be used as an indicator of the existence of cannabis effects in rats and is useful when very low doses are involved.

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