Effects of Acute and Chronic Administration of Cannabis Sativa and \((--)(\Delta^9)^\text{trans}\)-Tetrahydrocannabinol on the Behavior of Rats in an Open-Field Arena*

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Abstract. The effects of acute and chronic administration of \(\Delta^9\)-THC, cannabis extract and control solution on the behavior of rats repeatedly exposed to an open-field arena have been studied. After the first dose both \(\Delta^9\)-THC and cannabis extract significantly decreased defecation, grooming and rearing; ambulation was not affected. After 20 injections of both marihuana compounds the rats showed values for defecation, grooming and rearing near to those obtained during the pre-drug phase; control rats, however, showed a significant decrease in these parameters indicating habituation to the open-field. The results are discussed in terms of effects of marihuana on emotional behavior of rats.

Key-Words: Marihuana — \(\Delta^9\)-Tetrahydrocannabinol — Emotional Behavior — Habituation.

The responses of laboratory animals to marihuana and \((--)(\Delta^9)^\text{trans}\)-tetrahydrocannabinol (\(\Delta^9\)-THC) seem to depend upon the schedule of drug administration. Acute administration provokes, among others, the following effects: a) delay in climbing rope performance of rats (Carlini, 1968), b) decrease of bar pressing behavior of rats (Silva et al., 1968), c) decrease of spontaneous motor activity of mice (Holtzman et al., 1969; Carlini et al., 1970), d) potentiation of hexobarbital sleep-time (Garriot et al., 1967), e) catatonic-like state in mice and rats (Carlini et al., 1970; Grunfeld and Edery, 1969), f) suppression of isolated-, induced fighting behavior of mice (Santos et al., 1966; Salustiano et al., 1966), g) decrease of key pecking behavior of pigeons (Siegel, 1969), h) analgesic effect on mice (Bicher and Mechoulan, 1968), i) suppression of conditioned avoidance responses in rats (Grunfeld and Edery, 1969) and j) alteration of maze performance of rats (Carlini and Kramer, 1965;

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Carlini et al., in press). Most, if not all, of these effects are also observed with central nervous system depressant drugs, including tranquilizing agents. On the other hand, it has been reported that chronic administration of marihuana does not produce the effects \(a\), \(b\), \(g\) and \(j\), because of development of tolerance (Carlini, 1968; Silva et al., 1968; Carlini et al., in press; Frankenheim et al., 1970). Furthermore, when cannabis extract or \(\Delta^9\)-THC are given chronically to starved rats, the initial depressive effects wear off after a few daily injections, giving place to irritability and aggressive behavior (Carlini and Masur, 1969; Carlini and Masur, 1970).

These data seem to indicate that marihuana and \(\Delta^9\)-THC might have two different types of action. An acute, depressant action, which subsides rapidly after a number of injections, and effects such as irritability and aggressive behavior which could be better disclosed after tolerance to the former action has developed.

The present work was undertaken in an attempt to shed some light on this subject. Rats were submitted to daily injections of a marihuana extract and \(\Delta^9\)-THC and exposed periodically to an open field arena. This method has been used for many years and it is generally accepted that it measures “emotionality” in the rat (Hall, 1934; Brimblecombe, 1963; Broadhurst, 1969; Denenberg, 1969).

Methods

Drugs. Cannabis extract obtained from plants cultivated in the Northeast of Brazil (Mato Grosso State) was prepared and suspended in saline plus tween-80 as described by Carlini and Kramer (1965). Suspensions of \(\Delta^9\)-THC and the control solution consisting of saline plus tween-80 were prepared in the same way.

Animals. 117 male and female Wistar rats, 70 day old at the beginning of the experiment, were used. Since weaning at 30 days, the animals were housed in groups of five in wooden cages measuring 48 × 28 × 20 cm. Daily handling of the rats consisted of cleaning the cages and providing food and water every morning. All trials were performed in the afternoon.

Apparatus. The open-field arena was constructed according to Broadhurst (1960). It consisted of an arena of plywood measuring 85 cm in diameter and surrounded by a curtain of two layers of muslin. Three 60 watt lamps and three loudspeakers giving a constant white noise of 76 decibels were suspended, respectively, 110 and 140 cm from the floor.

Procedure. The experiment was carried out in two phases. In the first phase only female rats were used; 1 month later the male rats were tested. At the age of 70 days the animals were exposed to the open-field for 2 consecutive days, 3 min a day (exposure 1 and 2). The number of