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A vapourized Δ(9)-tetrahydrocannabinol (Δ(9)-THC) delivery system part II: comparison of behavioural effects of pulmonary versus parenteral cannabinoid exposure in rodents.

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Abstract

INTRODUCTION: Studies of the rewarding and addictive properties of cannabinoids using rodents as animal models of human behaviour often fail to replicate findings from human studies. Animal studies typically employ parenteral routes of administration, whereas humans typically smoke cannabis, thus discrepancies may be related to different pharmacokinetics of parenteral and pulmonary routes of administration. Accordingly, a novel delivery system of vapourized Δ(9)-tetrahydrocannabinol (Δ(9)-THC) was developed and assessed for its pharmacokinetic, pharmacodynamic, and behavioural effects in rodents. A commercially available vapourizer was used to assess the effects of pulmonary (vapourized) administration of Δ(9)-THC and directly compared to parenteral (intraperitoneal, IP) administration of Δ(9)-THC.

METHODS: Sprague-Dawley rats were exposed to pure Δ(9)-THC vapour (1, 2, 5, 10, and 20mg/pad), using a Volcano® vapourizing device (Storz and Bickel, Germany) or IP-administered Δ(9)-THC (0.1, 0.3, 0.5, 1.0mg/kg), and drug effects on locomotor activity, food and water consumption, and cross-sensitization to morphine (5mg/kg) were measured.

RESULTS: Vapourized Δ(9)-THC significantly increased feeding during the first hour following exposure, whereas IP-administered Δ(9)-THC failed to produce a reliable increase in feeding at all doses tested. Acute administration of 10mg of vapourized Δ(9)-THC induced a short-lasting stimulation in locomotor activity compared to control in the first of four hours of testing over 7days of repeated exposure; this chronic exposure to 10mg of vapourized Δ(9)-THC did not induce behavioural sensitization to morphine.

DISCUSSION: These results suggest vapourized Δ(9)-THC administration produces behavioural effects qualitatively different from those induced by IP administration in rodents. Furthermore, vapourized Δ(9)-THC delivery in rodents may produce behavioural effects more comparable to those observed in humans. We conclude that some of the conflicting findings in animal and human cannabinoid studies may be related to pharmacokinetic differences associated with route of administration.

KEYWORDS: Cross-sensitization; Food consumption; Locomotion; Pulmonary administration; Rat; Δ(9)-Tetrahydrocannabinol (Δ(9)-THC)

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