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"Effects of Cannabinoids and a Cannabinoid Extract on Thermal Nociception and Conditioned Behavior"

Introduction: Cannabinoids have been considered as alternatives to opioids, and therefore, have been tested for their antinociceptive effects and potential as analgesics. Our research aimed to examine the antinociceptive and behavioral effects of Δ^9 -tetrahydrocannabinol (Δ^9 -THC), Δ^{8} -THC, (-)-CP 55.940 (CP), and a cannabis-derived mixture (NEPE14). **Methods**: Nine male Sprague Dawley rats were trained to respond under a fixed-ratio 30 schedule (FR-30), with food pellets serving as the reinforcer. Overall response rate, running rate, and pre-ratio pauses were recorded during each session. Following the session, nociception was analyzed using warm-water tail-withdrawal latency (measured in seconds) in either 40 or 50 °C water. Thirty minutes prior to the session, subjects were administered the cannabinoids or NEPE14 twice per week (Tuesday and Friday) along with a control injection once per week (Thursday). Each substance was administered until complete dose-effect curves were established. Results: Acute Δ^{9} -THC, Δ^{8} -THC (1-5.6 mg/kg) and CP (0.032-0.18 mg/kg) significantly and dosedependently decreased overall response rate and running rate; PRP was not affected Both THC isomers and CP also increased tail-withdrawal latency compared to vehicle. In contrast, NEPE14 (3.7-20.7 ml/kg i.p.) did not significantly decrease response rates or increase tailwithdrawal latency even though the volumes administered contained doses of Δ^{9} -THC that had effects alone. Conclusions: Unlike the cannabis mixture NEPE14, the two THC isomers and CP significantly reduced thermal nociception, suggesting these cannabinoids may by effective for treating some types of pain. However, only CP produced antinociceptive effects that were more potent than their disruptive effects on conditioned behavior.