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"An Evaluation of the Antinociceptive and Behaviorally-Disruptive Effects of delta-9-tetrahydrocannabinol in Sprague Dawley Rats"

As the dangerous and addictive effects of opioids have become more widely recognized, researchers are investigating many novel alternative drugs for mitigating pain. Cannabinoids, specifically delta-9-tetrahydrocannabinol (THC), are among the most popular of these alternatives. However, while THC can produce antinociceptive effects (i.e., reduce pain), it can also produce disruptions in conditioned behaviors. Our experiments were conducted to directly compare and contrast the antinociceptive and behaviorally-disruptive effects of THC in outbred Sprague Dawley rats.

To assess the effects of THC on conditioned behavior, nine subjects were trained to respond under an operant schedule of reinforcement. More specifically, subjects responded under a fixed-ratio 30 (FR-30) schedule of food pellet presentation; that is, every 30 responses on a response lever in the presence of a red stimulus resulted in the presentation of one food pellet. Behavioral sessions lasted 60 minutes and were conducted five days per week. After the behavioral sessions, thermal antinociception was tested by dipping the rats' tails in either 40 or 50 °C water and measuring the tail-withdrawal latency from both water temperatures. The effects of THC on both conditioned behavior and nociception were tested by acutely injecting single doses 30 min prior to these procedures one to two times per week until an entire dose-effect curve was established. THC vehicle was also injected once per week as a control.

Training of the subjects resulted in both stable response rates under the FR schedule of food reinforcement and consistent tail-withdrawal latencies from the 40 or 50 °C water. Typically, subjects were able to maintain their tails in the 40 °C water for the maximum latency of 20 seconds, whereas the mean latency for tail withdrawal from the 50 °C water was 8.45 seconds. Following the administration of 1-5.6 mg/kg of THC, responding under the FR-30 schedule was dose-dependently decreased and tail-withdrawal latency from 50 °C was increased. For example, the 5.6 mg/kg dose decreased response rate from 1.37 under control conditions to 0.23 responses per second, while tail-withdrawal latency was increased from 8.45 to 19.15 seconds.

Together, these data indicate that THC can reliably produce thermal antinociceptive effects, but that these effects are produced at doses that either markedly decrease or eliminate conditioned behavior.