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## Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability.

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### Abstract

Cannabinoids combined with opioids produce synergistic antinociceptive effects, decreasing the lowest effective antinociceptive opioid dose (i.e., opioid-sparing effects) in laboratory animals. Although pain patients report greater analgesia when cannabis is used with opioids, no placebo-controlled studies have assessed the direct effects of opioids combined with cannabis in humans or the impact of the combination on abuse liability. This double-blind, placebo-controlled, within-subject study determined if cannabis enhances the analgesic effects of low dose oxycodone using a validated experimental model of pain and its effects on abuse liability. Healthy cannabis smokers (N = 18) were administered oxycodone (0, 2.5, and 5.0 mg, PO) with smoked cannabis (0.0, 5.6%  $\Delta^9$  tetrahydrocannabinol [THC]) and analgesia was assessed using the Cold-Pressor Test (CPT). Participants immersed their hand in cold water (4 °C); times to report pain (pain threshold) and withdraw the hand from the water (pain tolerance) were recorded. Abuse-related effects were measured and effects of oxycodone on cannabis self-administration were determined. Alone, 5.0 mg oxycodone increased pain threshold and tolerance ( $p \leq 0.05$ ). Although active cannabis and 2.5 mg oxycodone alone failed to elicit analgesia, combined they increased pain threshold and tolerance ( $p \leq 0.05$ ). Oxycodone did not increase subjective ratings associated with cannabis abuse, nor did it increase cannabis self-administration. However, the combination of 2.5 mg oxycodone and active cannabis produced small, yet significant, increases in oxycodone abuse liability ( $p \leq 0.05$ ). Cannabis enhances the analgesic effects of sub-threshold oxycodone, suggesting synergy, without increases in cannabis's abuse liability. These findings support future research into the therapeutic use of opioid-cannabinoid combinations for pain.

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