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Synergistic affective analgesic interaction between delta-9-tetrahydrocannabinol and morphine

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Abstract

Evidence for an analgesic interaction between delta-9-tetrahydrocannabinol (Δ^9-THC) and morphine was sought using an experimental pain model applied to normal volunteers. The study incorporated a double blinded, four treatment, four period, four sequence, crossover design. Subjects received Δ^9-THC 5 mg orally or placebo and 90 min later morphine 0.02 mg/kg intravenously or placebo. Fifteen minutes later subjects rated the pain associated with the application of thermal stimuli to skin using two visual analog scales, one for the sensory and one for the affective aspects of pain. Among sensory responses, neither morphine nor Δ^9-THC had a significant effect at the doses used, and there was no significant interaction between the two. Among affective responses, although neither morphine nor Δ^9-THC had a significant effect, there was a positive analgesic interaction between the two ($p = 0.012$), indicating that the combination had a synergistic affective analgesic effect. The surprisingly limited reported experimental experience in humans does not support a role for Δ^9-THC as an analgesic or as an adjunct to cannabinoid analgesia, except for our finding of synergy limited to the affective component of pain. Comparison of our results with those of others suggests that extrapolation from experimental pain models to the clinic is not likely to be a straight-forward process. Future studies of Δ^9-THC or other cannabinoids in combination with opiates should focus upon clinical rather than experimental pain.

Keywords

- Narcotics;
- Opioid;
- Cannabinoid;
- Pain

Figures and tables from this article:

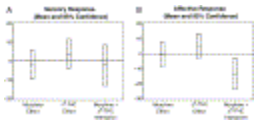

Fig. 1. Single agent effects and dual agent interactions of morphine and Δ⁹-THC upon sensory (A) and affective (B) pain responses to a painful stimulus. Effects calculated using the average response per subject minus the average baseline response. Interactions calculated from a mixed-effects model as described in Methods. Vertical axis represents displacement of responses on a scale of 100 mm.

Figure options

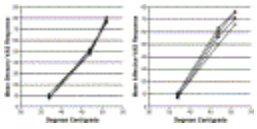

Fig. 2. Mean sensory and affective responses at three thermal stimulus temperatures. Conditions are: placebo/placebo (♦), placebo/morphine (▪), Δ⁹-THC/placebo (▴), Δ⁹-THC/morphine (×).

Figure options

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