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Effects of repeated morphine on intracranial self-stimulation in male rats in the absence or presence of a noxious pain stimulus.

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Abstract: Research on opioid analgesics such as morphine suggests that expression of abuse-related effects increases with repeated exposure. Repeated exposure to opioids often occurs clinically in the context of pain management, and a major concern for clinicians is the risk of iatrogenic addiction and dependence in patients receiving opioids for treatment of pain. This study compared abuse-related morphine effects in male rats in an intracranial self-stimulation (ICSS) procedure after repeated treatment either with morphine alone or with morphine in combination with a repeated noxious stimulus (intraperitoneal administration of dilute acid). The study also permitted comparison of morphine potency and effectiveness to block acid-induced depression of ICSS (antinociception) and to produce enhanced facilitation of ICSS (abuse-related effect). There were 3 main findings. First, initial morphine exposure to drug na?ve rats did not produce abuse-related ICSS facilitation. Second, repeated daily treatment with 3.2 mg/kg/day morphine for 6 days increased expression of ICSS facilitation. This occurred whether morphine was administered in the absence or presence of the noxious stimulus. Finally, a lower dose of 1.0 mg/kg/day morphine was sufficient to produce antinociception during repeated acid treatment, but this lower dose did not reliably increase abuse-related morphine effects. Taken together, these results suggest that prior morphine exposure can increase abuse liability of subsequent morphine treatments even when that morphine exposure occurs in the context of a pain state. However, it may be possible to relieve pain with relatively low morphine doses that do not produce increases in abuse-related morphine effects.