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Mu Opiod Receptor Desensitization in Inflammatory Pain

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Due to the epidemic level of opioid overdose deaths in the United States, improving the treatment of chronic pain has become a pressing concern. Opioid treatments such as fentanyl and morphine activate mu opioid receptors (MORs), causing an increase in dopamine release. Long-term use of opioids, even as prescribed by a physician, can desensitize the MORs and lead to the appearance of withdrawal symptoms when the receptors are no longer stimulated. Since pain increases endogenous opioid release, we hypothesized that this increase may cause MOR desensitization and the appearance of withdrawal syndrome upon blockade of MORs, as seen in long-term opioid use. To test this hypothesis, we bilaterally inserted cannulae into the ventral tegmental area (VTA), a region containing MORs and involved in reward processing, of Sprague-Dawley and Long-Evans rats of both sexes. Complete Freund's Adjuvant (CFA) was used to induce chronic inflammatory pain. CTAP, a highly selective MOR antagonist, was injected via cannulae to induce withdrawal symptoms. Each animal experienced one of three conditions: CFA + CTAP, Saline + CTAP, or CFA + Saline. Wet dog shakes (WDS), a common sign of opioid withdrawal in rats, were measured in five-minute periods one, two, three, five, and eight hours after CTAP injection. Significant increases in WDS were observed for male Sprague-Dawley rats in the CFA+CTAP group compared to the other conditions. This increase in WDS may be explained by chronic pain causing MOR desensitization in the same manner as long term exposure to opioids. More work investigating how pain impacts opioid dependent dopamine release is necessary and may ultimately lead to improved pain treatment and decreased opioid dependence.