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DISSECTING THE KAPPA OPIOID RECEPTOR SYSTEM IN PAIN INDUCED NEGATIVE AFFECTS

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The dynorphin–kappa-opioid receptor (KOR) system produces anhedonia, depressive states and decrease goal-driven motivation, some of the characteristics often reported in patients experiencing pain conditions. Recent evidences have demonstrated that this dynorphin–KOR system in the nucleus accumbens (NAc), a brain structure deeply involved in reward and aversion, plays a major role in the regulation of reinforcing properties and motivation. In this structure stimulation of KOR by dynorphin decreases reward-induced release of dopamine, a neurotransmitter deeply involved in positive reinforcement. Therefore, we hypothesized that this dynorphin–KOR system might represent a necessary and sufficient system to explain the opioid misuse observed in patients experiencing chronic pain. To test our assumption, we primarily studied how pain impacts opioid self-administration in a rat model. After acquiring self-administration behavior using sucrose pellets, rats were implanted with an intra-jugular catheter and, after recovery from the surgery, were exposed to a daily two-hour session of fentanyl self-administration for two weeks. After the animals demonstrate a consistent fentanyl intake, known as a hedonic spot, we induced inflammatory pain using a complete Freund's adjuvant injection in the right hind paw and measured, 48 hours later, the amount of fentanyl consumed by rats experiencing inflammatory versus controls (no pain). Our results showed no changes in the overall consumption; however, the animals experiencing inflammatory pain present bursts of fentanyl self-administration during the session whereas our control animals present a linear and consistent drug consumption. Our result demonstrates for the first time a clear dissociation in how pain affects fentanyl use. With the current opioid epidemic in the U.S., the model we describe here could help future behavior research to better understand the key factors contributing to the opioid misuse epidemic.