Buprenorphine Blocks Cocaine Intake in Rodents through Activation of the Nociceptin/Orphanin FQ-NOP Receptor System

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Buprenorphine is a partial agonist at mu-opioid and NOP receptors. It has mixed but primarily antagonistic actions on kappa-opioid and delta-opioid receptors. Buprenorphine's effect on the reduction of alcohol, heroin and cocaine administration is well documented. Because of its opioid agonist effects, buprenorphine is abusable, therefore naloxone a mu-opioid receptor competitive antagonist is added in order to decrease the likelihood of abuse of the product. Although the in vivo properties of buprenorphine have been characterized, the underlying pharmacology and signaling, particularly in cocaine addiction, remains poorly understood and need more extensive pharmacological evaluation in vivo.

Here we sought interesting to investigate in rodents, whether the potential reduction of cocaine intake induced by buprenorphine was mediated via activation of NOP receptors.

Rats trained to self-administer cocaine 2 hours/day were injected with buprenorphine (0.3, 1 and, 3.0 mg/kg) intraperitoneally 90 min before access to cocaine. The effect of Naltrexone (0.25, 1.0 and 2.0 mg/kg) and of the selective NOP antagonist SB-612111 (10.0 and 30.0 mg/kg) was also tested on cocaine self-administration. The effectiveness of Naltrexone and of SB-612111 on the reduction of cocaine self-administration induced by Buprenorphine was subsequently explored. In conclusion, the concomitant administration of Naltrexone and SB-612111 was tested on the blockade of cocaine intake in rats induced by buprenorphine.

Here we confirmed that buprenorphine decreased cocaine self-administration in rats in a dose dependent manner. Naltrexone and the selective NOP antagonism SB-612111 did not affect cocaine self-administration per se. The co-administration of each single drug with buprenorphine failed to alter the reduction of cocaine intake in rats induced by buprenorphine while the concomitant administration of Naltrexone and SB-612111 completely reversed the buprenorphine blockade of cocaine self-administration.

Taken together, these data lead to suggest that drugs with a NOP agonistic and mu-opioid agonistic profile, can decrease cocaine self-administration with minimal liability to produce opioid dependence and may be useful as a treatment for cocaine addiction.