Published in final edited form as:

Biol Psychiatry. 2007 September 15; 62(6): 702.

Letter to the Editor

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I would like to suggest an extension to the intriguing proposal by Ciccocioppo et al. (1) that high-dose buprenorphine reduces alcohol drinking by acting as an agonist/partial agonist at the nociceptin/orphanin FQ (NOP) receptor. Several clinical trials have found that high-dose (12-16 mg daily as sublingual solution, bioequivalent to 24-32 mg as tablet) buprenorphine significantly reduces cocaine use by dually opiate- and cocaine-dependent outpatients (2;3). This effect is not seen at lower doses, at which buprenorphine's mu-opioid receptor agonist action would predominate (4). I suggest that buprenorphine's anti-cocaine effect at high doses, like its anti-alcohol effect, may also be mediated by activation of the NOP receptor.

I am not aware of any human data directly relevant to this proposal, but there are some suggestive animal data. Activation of NOP receptors in rodents, by intracerebroventricular administration of nociceptin, reduces the acquisition and expression of cocaine-induced conditioned place preference (5;6) and blocks cocaine-induced sensitization (7). In addition, such nociceptin administration reduces cocaine-induced dopamine release in the nucleus accumbens (8). These findings suggest that activation of NOP receptors, such as by high-dose buprenorphine, reduces the rewarding effects of cocaine, and thus might account for the anti-cocaine effect of high-dose buprenorphine.

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Financial Disclosure:

The author has no competing financial interests to declare.

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