CHRONIC COCAINE ADMINISTRATION ATTENUATES DELTA-OPIOID RECEPTOR FUNCTION IN FEMALE RATS
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The striatum receives dopaminergic input from midbrain projection neurons and is associated with cocaine-induced locomotion and reinforcement. These behaviors are mediated via interactions between dopamine and opioid systems. In males, chronic cocaine administration results in attenuation of the ability of the delta opioid receptor (DOR) agonist D-Pen2, D-Pen5-enkephalin (DPDPE) to inhibit adenylyl cyclase activity in the nucleus accumbens and caudate putamen (Unterwald, 1993). This effect is thought to be mediated by dopamine-D1 receptor (D1R) since the D1R agonist, SKF 82958, also attenuates delta opioid receptor-inhibited cyclase activity (Unterwald, 2001). Despite evidence showing sex differences in cocaine-induced behavioral sensitization, reinforcement and reward, there is little research focusing on the mechanisms underlying these differences. The present study investigated the effects of chronic cocaine administration on DOR receptor function in female rats. Female rats received three daily intraperitoneal injections of cocaine in a binge-pattern for 14 days followed by one-day withdrawal from the drug. Adenylyl cyclase activity was measured in the nucleus accumbens and caudate putamen ex vivo in response to increasing concentrations of DPDPE. Chronic cocaine attenuated the ability of DPDPE to inhibit adenylyl cyclase activity in striatal regions. These results demonstrate that females, similar to males, exhibit a decrease in DOR function following chronic cocaine administration, which may contribute to the anxiogenic responses induced by chronic cocaine. Future studies focusing on the hormonal fluctuations during the rat estrous cycle are essential in order to elucidate the mechanisms underlying sex differences in response to cocaine.