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Role of Serotonin 5-HT_{2A} and 5-HT_{2C} Receptors on the Reward-facilitating Effect of Cocaine

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INTRODUCTION

The serotonin 5-HT_{2A} and 5-HT_{2C} receptors, which are found in abundance in the mesolimbocortical dopaminergic system, appear to modulate the behavioral effects of cocaine. The present series of studies set out to investigate the role of 5-HT_{2A} and 5-HT_{2C} receptors on the reward-facilitating effect of cocaine and localize the neural substrates within the mesolimbo-cortical dopaminergic system that are responsible for these effects.

METHODS

Male Sprague-Dawley rats were implanted with stimulating electrodes and bilateral cannulae for the experiments involving microinjections and were trained to respond for electrical stimulation. In the first study we examined the effectiveness of systemic administration of selective 5-HT_{2A} and 5-HT_{2C} receptor agonists (TCB-2 and WAY-161503) and antagonists (R-96544 and SB-242084) at blocking the reward-facilitating effect of cocaine. In the second study we examined the effects of intra-medial prefrontal cortex (mPFC), intra-nucleus accumbens (NAC) and intra-ventral tegmental area (VTA) injection of WAY-161503 on the reward-facilitating effect of cocaine.

RESULTS

Systemic WAY-161503 attenuated the reward-facilitating effect of cocaine. This effect was reversed by pre-treatment with the selective 5-HT_{2C} receptor antagonist SB-242084. Intracranial micro-injections of WAY-161503 into the mPFC and the NAC shell/core, but not the VTA, attenuated the reward-facilitating-effect of cocaine.

CONCLUSION

These data indicate that 5-HT_{2C} receptors within the mPFC and the NAC modulate the reinforcing effects of cocaine and provide evidence that 5-HT_{2C} receptor agonists could be a possible drug discovery target for the treatment of psychostimulant addiction.

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