

## **Withdrawal from chronic cocaine**

### **Stress-induced suppression of the immune system after withdrawal from chronic cocaine.**

**Avila AH, Morgan CA, Bayer BM.**

Department of Pharmacology, Georgetown University Medical Center, Washington, DC 20057, USA.

Recent evidence suggests that withdrawal from cocaine shares similarities to the stress response. Here, we examine whether withdrawal from chronic cocaine produces immune system alterations and whether the hypothalamic-pituitary-adrenal axis is involved. Sprague-Dawley male rats received cocaine (10 mg/kg i.p., b.i.d.) or saline, followed by 2 h, 1, 2, 4, 6, and 14 days of withdrawal. Proliferation responses of peripheral blood lymphocytes to concanavalin A were significantly suppressed at the 2-h, 1- and 2-day time points, and persisted for up to 6 days during withdrawal from chronic cocaine. Flow cytometric analysis revealed no significant differences in the immunophenotype of blood lymphocytic populations of T cells, B cells, or monocytes at 2 or 6 days of withdrawal from cocaine. Consistent with the suppression in cellular immunity observed in the *in vitro* response, the *in vivo* delayed-type hypersensitivity response was also significantly decreased in cocaine withdrawing animals. Plasma corticosterone levels were significantly elevated 2 and 24 h after cessation of cocaine but returned to basal values by 2 days of withdrawal. The suppressive effects of cocaine withdrawal were no longer observed in either adrenalectomized animals or those treated with the glucocorticoid receptor antagonist mifepristone (RU486), when administered during the first 2 days of withdrawal. These data argue that repeated exposure to cocaine followed by withdrawal leads to an activation of the neuroendocrine stress response, which alters cellular immunity during the initial withdrawal phase and may contribute to an increased susceptibility to infection.

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