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Short communication

Effects of cortisol and cocaine on plasma prolactin and growth hormone levels in cocaine-dependent volunteers

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Abstract

In rodents, corticosterone (cortisol in humans) facilitates cocaine self-administration purportedly via enhancement of dopaminergic activity in the brain. This study sought to assess central dopaminergic effects of cortisol in humans and to compare them to those of cocaine. Twelve cocaine-dependent individuals received an intravenous bolus of cortisol (0.5 and 0.2 mg/kg; n=6 for each dose) and cocaine (0.2 mg/kg) in a double-blind randomized placebo-controlled and counterbalanced fashion. Their plasma was assayed over the next 120 min for prolactin and growth hormone (GH), which are two neuroendocrine indices of dopaminergic function. Cortisol injections produced significant increases in GH, while cocaine resulted in significant decreases in prolactin. Placebo administration was associated with gradual declines in prolactin, but the levels at the 90- and 120-min time points were significantly lower after cocaine than after placebo infusion. These different neuroendocrine response profiles point to important differences between dopaminergic effects of cortisol and cocaine.

Keywords: Cocaine; Cortisol; Reward; Euphoria; Reinforcement; Craving

1. Introduction

Several lines of evidence suggest that the primary glucocorticoid hormone, cortisol (corticosterone in rodents), plays a role in the course of cocaine dependence. Cocaine (Mello

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& Mendelson, 1997) and cocaine-related environmental cues are associated with robust elevations in plasma cortisol levels, while stress-induced hypercortisolemia was potentially related to cocaine craving (Sinha, Catapano, & O'Malley, 1999).

Moreover, studies in rodents suggested that similar to cocaine corticosterone increases dopamine release within the brain reward circuitry (Piazza et al., 1996). This feature may explain corticosterone's reinforcing effects, i.e., its own self-administration or its facilitation of acquisition, maintenance, and reinstatement of cocaine intake (Goeders 2002). Alternative reinforcing mechanisms of corticosterone may involve enhanced sensitivity of dopamine receptors (Goeders 2002), effects on other (than dopamine) neurotransmitters, and conditioned stimulus created by repeated pairing with cocaine use.

Contrary to the abovementioned findings in rats and clinical evidence demonstrating euphorogenic (i.e., rewarding) effects of cortisol (Plihal, Krug, Pietrowsky, Fehm, & Born, 1996), prior monkey (Broadbear, Winger, & Woods, 1999; Lee, Tiefenbacher, Platt, & Spealman, 2003) and human (Ward, Collins, Haney, Foltin, & Fischman, 1999; Kosten, Oliveto, Sevarino, Gonsai, & Feingold, 2002) studies, employing either cortisol synthesis blockade with ketoconazole or exogenous cortisol administration, reported no discernable effect on the reinforcing profile of cocaine. These negative findings led us to question whether corticosterone's dopaminergic activity observed in rodents could be extended to humans. To explore this issue, we compared the effects of cortisol versus cocaine infusion on indirect indices of central dopaminergic activity-plasma levels of prolactin and growth hormone (GH) in a sample of cocaine-dependent nontreatment seekers.

2. Methods

Twelve individuals (mean age±standard deviation: 39.8±3.5 years; weight: 79.9±13.6 kg; 3 females and 9 males; 4 Caucasian and 8 African-American) meeting DSM-IV criteria for cocaine dependence were recruited by advertisement and gave written informed consent to the Massachusetts General Hospital (MGH) IRB-approved protocol. The behavioral and cortisol data are described elsewhere (Elman, Lukas, Karlsgodt, Gasic, & Breiter, 2003) and were included in this report to allow more comprehensive description of the subjects' responses.

The subjects were in good physical health and had no past or current other Axis I psychiatric diagnosis besides alcohol and/or marijuana abuse. All subjects were active cocaine users (confirmed by a urinalysis) and were not seeking or participating in addiction treatment. They primarily smoked cocaine for 19.9±8.8 years, using 6.5±7.4 times in the month prior to study, with last use 1.4±1.1 days prior to the study.

At 9 a.m. on the day prior to the study, subjects were admitted to the MGH research unit, having refrained from cocaine for at least 10 h and completed medical work-up and structured clinical assessments. Those meeting all criteria were boarded overnight on the unit in preparation for infusions the following day. At 8 a.m. the following morning, the subjects had bilateral intravenous catheters placed (left forearm for infusions, right forearm for serial venous blood sampling). After a 60-min rest period, three infusions of either cocaine (0.2 mg/