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Enhanced Susceptibility of the Immune System to Stress in Morphine-Tolerant Rats

BARBARA M. BAYER, RENEE M. BREHIO, XUAN Z. DING, AND MONICA C. HERNANDEZ

Department of Pharmacology, Georgetown Medical School, Washington, DC

The purpose of the present study was to determine the potential consequences to the immune system of the combined exposure of rats to stressor and morphine. Within 30 min following either morphine (5 mg/kg) injection or restraint stress (30 min) maximal analgesic responses as measured by tail-flick assay were observed. However, only morphine treatment was accompanied by a significant suppression (50%) in mitogen-stimulated lymphocyte proliferative responses. Restraint stress for either a 30-min or 2-h duration had no effect on lymphocyte responses. Exposure to a combination of restraint stress and acute morphine (5 mg/kg) resulted in a 50% suppression of lymphocyte responses which was similar in magnitude to that observed with morphine administration alone. When rats were injected twice daily for 4 days with increasing doses of morphine ranging from 10 mg/kg to 40 mg/kg, morphine (10 mg/kg) administration on Day 5 was not accompanied by either analgesia or depressed blood lymphocyte proliferative responses. These results indicated that tolerance had developed to both the analgesic and the immunosuppressive effects of morphine. However, upon exposure of morphine-tolerant animals to restraint stress, significant analgesic responses were retained. Furthermore, in contrast to the lack of suppression following restraint stress on lymphocyte responses in saline-injected animals, restraint for 30 min produced greater than a 70% suppression in morphine-tolerant animals. These data suggest that morphine tolerance may be accompanied by an enhanced susceptibility to the immunosuppressive effects of stress. © 1994 Academic Press, Inc.

INTRODUCTION

As earlier stated very appropriately by Holpsapple and Munson (1985) "To date, few studies have determined the interactions between the repeated exposure to abused drugs and stress. Although the experimental design of this type of approach is difficult, it may be that such interactive studies would be the most sensitive indicators of the effects of drugs of abuse on immune responsiveness." The fact that intravenous drug users represent a major risk group for AIDS (Curran, Jaffe, Hardy, Morgan, Selik, & Dondero, 1988; Ginzburg, 1984) makes it imperative to understand these and other potential interactions between the effects of abused drugs and stress on the immune system.

Chronic exposure to morphine has been shown to effect a variety of immune parameters in both humans and animals. Heroin addiction is accompanied by an increased incidence of bacterial, protozoal, and viral infections (Briggs, McKerron, Souhami, Taylor, & Andrews, 1967; Hussey & Katz, 1950; Cherubin & Brown, 1968; Louria, 1974). Brown and colleagues were the first to observe a decreased mitogenic response to phytohemagglutinin (PHA), suggesting a defect in cell-mediated immunity (Brown, Stimmel, Taub, Kochwa, & Rosenfeld, 1974). Exposure of rodents to morphine has also been shown to be accompanied by a decrease in mitogenic responses (Ho & Leung, 1979; Bryant, Berton, & Holaday,

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