An unusual reaction to opioid blockade with naltrexone in a case of post-traumatic stress disorder

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An unusual behavioral and cardiovascular reaction was observed during opioid blockade with naltrexone in a 32-year-old male who met DSM III-R criteria for post-traumatic stress disorder (PTSD). As part of an ongoing placebo-controlled investigation of the effects of naltrexone on laboratory and ambulatory blood pressure reactivity, this participant reported experiencing feelings of rage, explosive behavior, and other unpleasant symptoms. When compared to all other subjects (N = 24), this individual showed significantly greater effects of naltrexone on blood pressure reactivity during the laboratory stressor. His ambulatory blood pressures, when compared to placebo, were significantly increased during the 24-hr period following naltrexone. The unusual behavioral and cardiovascular responses following ingestion of naltrexone suggest an important role for endogenous opioids in adjustment to stress in this case of PTSD.

KEY WORDS: post-traumatic stress disorder; endogenous opioids; ambulatory blood pressure; naltrexone; laboratory stress.

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INTRODUCTION

Post-traumatic stress disorder (PTSD) is a psychophysiologic disturbance that may arise following exposure to a traumatic event outside the range of usual human experience (American Psychiatric Association, 1987). Some of the characteristic symptoms of PTSD include, among others, reexperiencing the traumatic event(s), numbing of general responsiveness, periodic outbursts of anger, and increased arousal. Endogenous opioid peptides are released during intense stimulation and may be important in acute and chronic adaptation to traumatic stress (McCubbin, 1993). Van der Kolk and colleagues (1985) suggest that these neuropeptide systems may play a role in the development and maintenance of some of the characteristic symptoms of PTSD.

Evidence of opioidergic mechanisms in PTSD derive from several lines of research. For example, animal studies indicate that inescapable stress produces several symptoms that resemble the pathologic profile of PTSD, including analgesia, hyperarousal, and decreased motivation (Van der Kolk et al., 1985). Moreover, pharmacologic blockade of endogenous opioid receptors prevents stress-induced analgesia as well as the performance deficits that typically follow exposure to inescapable stress in rats (McCubbin et al., 1984). Similar effects have been observed in normal human subjects experiencing a perceived uncontrollable stressor (Bandura et al., 1988). Recently, the link between opioids and PTSD has been more directly examined by administration of naloxone to combat veterans with PTSD (Pitman et al., 1990). Combat veterans with PTSD showed decreased pain sensitivity following exposure to a dramatized combat movie. These analgesic effects were blocked with the short-term opioid antagonist naloxone, supporting the notion that endogenous opioids may be directly involved in the expression of PTSD symptomatology.

Our laboratory has been systematically examining the role of opioids in the expression of individual differences in circulatory, neuroendocrine, and behavioral reactivity to stress in young adults (McCubbin et al., 1985; McCubbin et al., 1989). Using pharmacologic blockade of endogenous opioids with naloxone, these studies have suggested that opioids can inhibit cardiovascular, sympathoadrenomedullary, and pituitary–adrenocortical reactivity, and moreover, this opioidergic inhibitory mechanism is diminished in persons at risk for cardiovascular disease. This research has recently been expanded to studies of the effect of the long-lasting oral opioid antagonist, naltrexone, on laboratory reactivity (McCubbin et al., 1992) and 24-hr ambulatory blood pressure patterns. We now report a case of an unusual behavioral and cardiovascular reaction during opioid blockade with naltrexone in a young adult male with a history of childhood abuse and military combat trauma who met DSM III-R criteria for PTSD.