In previous studies, we have shown that uncontrollable electrical stimulation attenuates the recovery of locomotor and bladder functions, and increases tissue loss after a contusion injury. An analgesic, systemic morphine, is not protective in this context and instead appeared to exacerbate the effects of shock. Moreover, independent of shock, morphine per se undermined the recovery of sensory function and produced symptoms of neuropathic pain. Rats treated with morphine alone also had significantly larger lesions than those treated with saline. These results are clinically important because they suggest that opiates may adversely affect the recovery of function.

We have now started to examine molecular changes that might contribute to the adverse effects of morphine and uncontrollable shock. Subjects were given a moderate contusion injury. The next day, after baseline locomotor function was assessed (BBB scale), they were injected with 20 mg/kg morphine (i.p.) or saline. Then, 30 min later, half of the subjects in each treatment group (n=8) were exposed to 6 min of shock, while the remaining subjects were restrained with no shock. Twenty-four hrs after treatment, locomotor performance was re-assessed, and subjects were euthanized. Trunk blood and a 5 mm segment of spinal cord tissue (centered over the lesion) were taken for analysis. Blood plasma was retained for determination of corticosterone concentrations using an ELISA (sensitivity = 26.99 pg/ml). Total protein was extracted from the spinal tissue and concentrations of the pro-inflammatory cytokines IL-1β and IL-6 were determined using ELISAs (sensitivity < 3 and 8 pg/ml, respectively).

There were significant effects of shock and morphine on corticosterone levels. Morphine also significantly increased IL-1β concentrations. The effects of morphine, and uncontrollable shock, therefore may depend in part on an elevation of corticosterone and/or IL-1β. Indeed, uncontrollable shock has been shown to elevate corticosterone levels in intact rats, and corticosterone exacerbates cell death in the hippocampus following injury. Pro-inflammatory cytokines, including IL-1β, are involved in the regulation of leukocyte recruitment and microglial activation in the early stage after a contusion injury, but they have also been linked to cytotoxic effects. We are now using an intrathecal model to further examine the interactions between the injured spinal system and morphine. The synergistic effects of morphine and uncontrollable nociceptive stimulation on corticosterone and IL-1β levels suggest, however, that a common mechanism may underlie the attenuation of recovery of function in both models.

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