Sex differences in the effect of stress on morphine antinociception and tolerance

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The purpose of this project was to determine if responses to acute and chronic morphine in male and female rats can be changed by stress. Intact and gonadectomized rats were exposed to three different stressors (swim, restraint, crowding) alternated daily for 6 days. Tolerance to morphine was induced with sustained-release morphine. Degree of tolerance was assessed by measuring the hot-plate latency. Eight withdrawal behaviors (escape/jump, rearing, wet-dog shake, teeth chatter, salivation-lacrimation-rhinorrhea (SLR), swallowing, irritability to touch, and grooming) were scored for 15 minutes after naloxone injection. Non-tolerant male rats had significantly higher morphine antinociception as compared to females, and this enhanced effect of morphine in males was further (two-fold) increased after stress. Stress did not change the antinociceptive effect of morphine in female rats. No sex differences were measured in tolerant rats. Profound differences in withdrawal behaviors occurred between males and females. Male rats showed significantly higher incidence of escape/jump, shake, rearing, and irritability to touch as compared to females. Females experienced predominantly symptoms of teeth chatter, swallowing, SLR, and tremor. Severity of male- and female-specific withdrawal symptoms was increased after stress. Incidence of some of the withdrawal behaviors was changed by gonadectomy. Results demonstrated that 1) stress increased antinociceptive effect of morphine in male rats and further potentiated the sex-specific difference in morphine antinociception, 2) there are sex-specific withdrawal behaviors that occur in rats tolerant to morphine & 3) severity of sex-specific withdrawal symptoms was increased by stress. [Supported by NSF-EPSCoR (#EPS-9350539)].