The opioid receptor mRNA expression and enhancement of tolerance development to morphine in rats prenatally exposed to morphine, methadone, and buprenorphine

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Heroin use among young women of reproductive age has drawn much attention around the world. However, there is a lack of information on long–term effects of prenatal exposure to opioids on their offspring. In this study, an animal model was established to study effects of prenatal exposure to opioids on the offspring. Female pregnant Sprague-Dawley rats were sub-grouped to receive (1) vehicle, (2) 2-4 mg/kg morphine (1 mg/kg increment per week), (3) 7 mg/kg methadone, and (4) 3 mg/kg buprenorphine, subcutaneously, once or twice a day from E3 to E20. The antinocicetive experiments were conducted on animals 8-12 weeks old and with body weight between 250 and 350 g. Results showed that prenatal exposure to buprenorphine caused higher mortality than other groups tested. Moreover, no obvious behavioral abnormality or body weight difference was noted during the growing period (8-12 weeks) in all offspring. When the male offspring received morphine injection twice a day for 4 days, the prenatally opioid-exposed rats more quickly developed tolerance to morphine, most notably the prenatally buprenorphine-exposed offspring. However, the tolerance development to methadone or

buprenorphine was not different in the offspring exposed prenatally to methadone or buprenorphine, respectively, when it was compared with the vehicle-controlled group. Similar results were also obtained in the female animals. In the mRNA expression study, the levels of mu-opioid and opioid like-1 receptor in periaqueductal gray region were markedly decreased after chronic morphine treatment on prenatally buprenorphine-exposed animals than other groups tested. This study indicates that buprenorphine in higher doses affects mRNA expression of these receptors.