Prenatal morphine exposure decreases analegsia but not K channel activation

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摘要

Abstract

The present study has investigated the possible supraspinal adaptive changes induced by prenatal administration of morphine, including morphine-induced supraspinal antinociception in vivo, the density and binding affinity of mu-opioid receptors in the brain and the cellular action of morphine in brain slices in vitro. The cellular action of morphine was assessed by its activation of K+ channels in the ventrolateral periaqueductal gray (PAG), a crucial area for the supraspinal analgesic effect of morphine. Female rats were treated with morphine 7 days before mating at 2 mg/kg. The treatment was continued during pregnancy and after delivery at doses which increased by 1 mg/kg every 2 weeks. Experiments were conducted in the offspring at p14 days. Prenatal morphine exposure induced tolerance to supraspinal morphine-induced tail-flick response. The binding affinity and maximal binding of [(3)H]DAMGO in whole brain were not significant different between the morphine- or saline-treated dams. Autoradiographic analysis shows that the mu-opioid receptor density was decreased in the striatum, thalamus and amygdala but not in the midbrain, nucleus accumbens, hippocampus or cortex in morphine offspring. In ventrolateral PAG neurons, morphine activated inwardly rectifying K+ channels in 59% of recorded neurons of morphine offspring. Neither the magnitude of K channel activation nor the percentage of sensitive neurons was different between the saline- and morphine-treated offspring. It is concluded that prenatal morphine exposure induces tolerance to supraspinal analgesia and this tolerance is not attributed to a change in the mu-opioid receptor density or the receptor-function coupling efficiency in the midbrain periaqueductal gray.