

Opioid ligands differentially affect self-administration in rats raised in different rearing environments during adolescence

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Most studies to date have established that rats raised in environmental enrichment through adolescence (enriched condition, EC) self-administer less stimulant drugs than rats raised in standard housing (standard condition, SC) and isolation housing (isolated condition, IC) [1,2]. One proposed mechanism for rearing environment-induced differences in stimulant self-administration is altered endogenous opioid signaling. EC (but not IC) rats engage in social play with their peers on a daily basis, an activity postulated to cause endogenous opioid release [4]. Over time, this could result in long-term alterations in opioid signaling that differ between EC and IC rats. Given the literature that endogenous opioid signaling contributes to reward-mediated behavior [3], this could explain the increased stimulant self-administration observed in IC rats.

Methods: The first study measured acquisition of self-administration of the short-acting opioid remifentanyl (1 or 3 $\mu\text{g}/\text{kg}$) in EC, SC, and IC rats. After acquisition, rats were allowed to administer several different doses of remifentanyl (0, 0.1, 0.3, 1, 3, and 10 $\mu\text{g}/\text{kg}$) in semi-random order to generate a dose-response curve for each group. For the second study, a separate group of EC and IC rats were trained to lever press for cocaine using a within-session demand procedure. This procedure measured cocaine consumption under changing cocaine price by decreasing the dose of cocaine earned throughout a 60-min session. Rats were able to self-administer cocaine on a FR1; every 10 min the cocaine dose was systematically decreased (0.75 - 0.003 mg/kg/infusion cocaine). After 10 days of training on this procedure, rats were randomly pretreated with 0, 0.3, 1, and 3 mg/kg morphine once every 3 days, followed by random pretreatments of 0, 0.3, 1, and 3 mg/kg naltrexone once every 3 days. Economic demand functions were fit to each rat's cocaine consumption from each pretreatment; best-fitting alpha and Q(o) parameters were extracted and analyzed.

Results: IC rats acquired self-administration more quickly than EC and SC rats and self-administered more remifentanyl than EC rats at both training doses. For study two, the data partially supported the hypothesis that IC rats are more sensitive to the effect of morphine pretreatment, as evidenced by larger alpha values after morphine. However, EC rats also consumed less cocaine after morphine pretreatment, reflected by lower Q(o) values.

Discussion: The current studies shed light on the role of adolescent rearing environment on opioid sensitivity in adulthood and suggest that the increased self-administration observed in IC rats may be caused by an opioid deficiency.

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