TLR4 ELIMINATION PREVENTS LONG-LASTING ETHANOL EFFECTS ON COCAINE-INDUCED CONDITIONED PLACE PREFERENCE IN ADOLESCENT MICE

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Our previous studies indicated that binge-like ethanol treatment in adolescent rats induces an increase in the conditioned rewarding effects of cocaine. Ethanol induces the production of cytokines and inflammatory mediators, that cause brain damage by activating the toll-like receptor 4 (TLR4) signaling response. To test if these receptor mediated the observed increased in cocaine-induced conditioned place preference (CPP) after adolescent ethanol exposure, we used wild-type (WT) and TLR4-deficient (TLR4-KO) adolescent mice treated intermittently with ethanol (3 g/kg) for 2 weeks, evaluating the CPP induce by 3 mg/kg of cocaine three weeks later. Morning doses (9–10 a.m.) of either saline or 25% (v/v) ethanol (3 g/kg) in isotonic saline were administered intraperitoneally to 30-day-old mice on 2 consecutive days with 2-day gaps without injections for 2 weeks (PND 30 to PND 43). Then, mice were maintained without alcohol treatment until PND 65, when the CPP started. The WT EtOH-exposed group developed preference for the this cocaine dose that required 12 sessions to be extinguished, and a priming dose of 1.5, 0.75 and 0.375 mg/kg of cocaine reinstated the preference, that needed 7, 4 and 10 more sessions respectively to be extinguished. In WT-saline treated and in KO animals (saline- or ethanol-treated), there was not observed any significant effect. These results support the role of the neuroimmune response and TLR4 signaling in the behavioral effects of ethanol in adolescence.


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