D-Penicillamine Prevents the Alcohol Deprivation Effect in the Operant Self-Administration Paradigm

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Although pharmacological treatments for relapse prevention have experienced some progress, their general effectiveness can be considered low and the problem could not be considered solved. In recent years, our group has explored the use of acetaldehyde (ACD) sequestering agents as a new and very promising strategy. These agents, such as D-Penicillamine (DP), may prevent the actions of ethanol-derived ACD on specific brain regions and pathways. In this sense, our previous studies have reported that DP is able to block relapse in alcoholism and the advantage of the combined use of DP with naltrexone (an approved treatment for relapse therapy but with reduced efficacy) relative to naltrexone alone. The effectiveness of treatments was evaluated through preclinical studies using the Alcohol Deprivation Effect (ADE) model. According to NIAAA recommendations to evaluate the preclinical efficacy of a potential anti-relapse treatment, the present study is aimed at investigating the reproducibility of our previous data in a different laboratory and under different experimental conditions. Thus, male Wistar rats with a limited (30 min sessions), intermittent and extended background of ethanol operant self-administration were used. The efficacy of several DP doses (6.25, 12.5 and 25 mg/kg i.p.) in preventing alcohol relapse, using a protocol based on the ADE, was evaluated. The effect of DP on rats spontaneous motor activity was also tested. Results showed a significant ADE in animals treated with saline, however DP treatment blocked the increase in ethanol responses following the imposed abstinence period. Furthermore, DP treatment did not modify the basal motor activity.