LOCAL BLOCKADE OF THE MU OPIOID RECEPTOR REVEALS THE DUAL MOTOR EFFECT OF ETHANOL IN pVTA


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Previous electrophysiological and behavioral data have revealed the existence of ethanol opposite effects (excitatory and inhibitory) on the posterior ventral tegmental area (pVTA) dopamine (DA) neurons activity. These activating and depressing effects of ethanol could be the result of two concurrent and opposing mechanisms, one increasing and the other reducing GABA release onto pVTA DA neurons. The activation observed after acute ethanol administration could be dependent on disinhibition mediated by salsolinol (an ethanol-derived metabolite) through interactions with mu-opioid receptors (MORs) existing on soma of VTA GABA neurons, whereas the ethanol non-metabolized fraction could be responsible for the depression of DA neurons through a mechanism involving GABA_A receptors. Indeed, the net effect of intra-VTA ethanol would be dependent on the balance between the activation and the depression effects induced by the metabolized and non-metabolized ethanol fractions. Different pharmacological strategies affecting the local ethanol metabolism have previously been used to disentangle this complex scenario. In the present study, we have explored these phenomena by using other alternative strategy: the blockade of MORs to suppress selectively the activating effects mediated by salsolinol without affecting the inhibitory effects mediated by the non-metabolized fraction of ethanol. The consequences of an ineffective dose of ethanol (35 nmol) after intra-VTA administration on the motor activity of rats were analyzed in animals under local and selective blockade of MORs with the antagonist β-Funaltrexamine (β-FNA). Results showed that the pretreatment with β-FNA selectively blocked the activating effects of ethanol leaving unaltered the concurrent depressing effect. Consequently, the initially ineffective 35 nmol dose of ethanol became a depressant dose.