Effects of histamine H3 receptor modulators on the sedative effects induced by ethanol.

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Introduction

Histaminergic system and its H_3 receptors (H3R) are involved in numerous (patho)physiological and higher brain functions. However, despite its central role, very few studies are available on the link between histamine, H3R, and ethanol-induced behaviours.

Therefore, the **rationale** of this study was to **explore the role of histamine and H3R in alcohol-induced sedation**. We assessed the actions of two H3R agonists, immepip and imetit, and of two H3R antagonists, thioperamide and A331440, on the loss of righting reflex (LORR) induced by ethanol in mice.

Methods

Animals

310 Female Swiss mice (8-10weeks) were used for the experiments.

Drugs

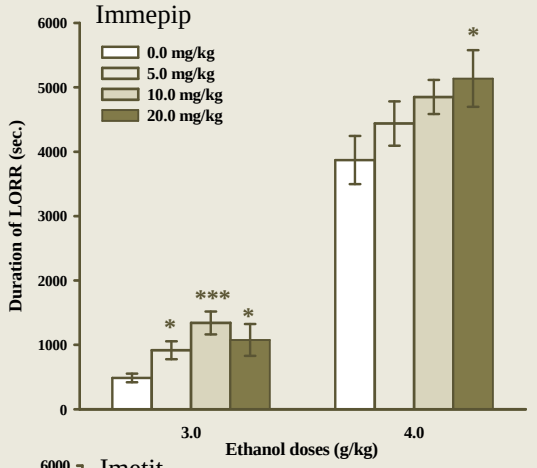
Alcohol injections (3.0-4.0 g/kg) were 20% (v/v), diluted from 99.99% ethanol with 0.9% saline solution Immepip(10.0-20.0mg/kg), imetit(5.0-20.0mg/kg), A331440(5.0-20.0mg/kg) and thioperamide(10.0-20.0mg/kg) were dissolved in 0.9% saline and injected at a volume of 0.01 ml/g of body weight. The various H3R modulators were injected (i.p.) 30 minutes before the ethanol injections.

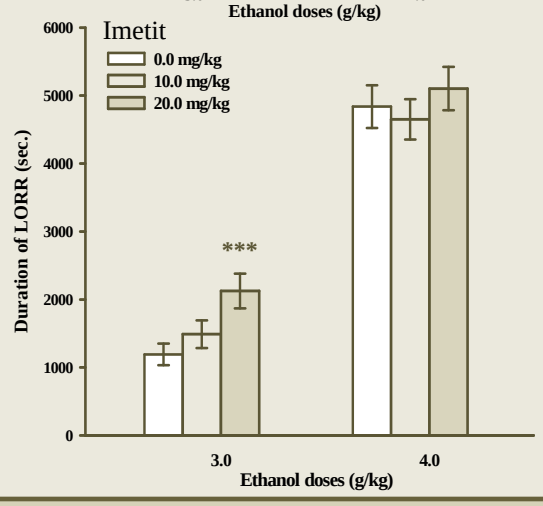
Sedation

To assess the sedative effects of alcohol, 3.0 and 4.0 g/kg of ethanol were injected and the duration of the induced LORR was measured

Results

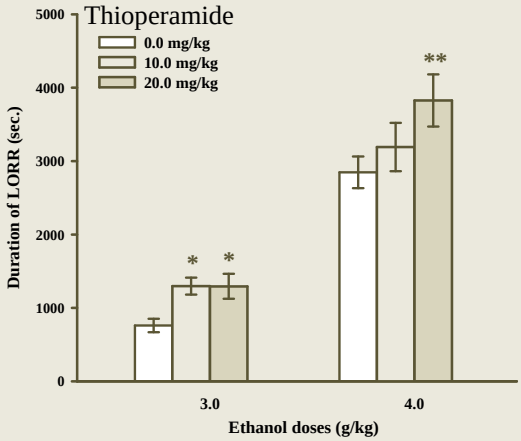
H3R agonists

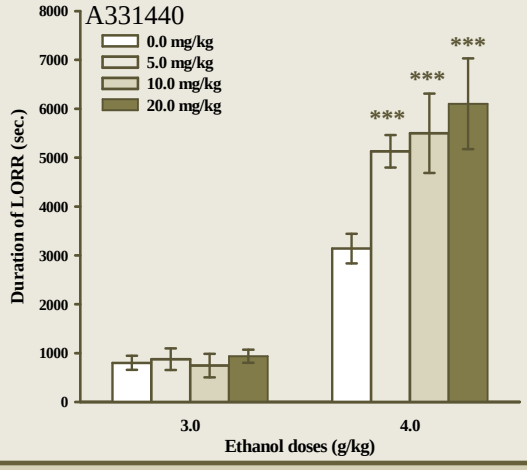




* p<0.05
** p<0.01
***p<0.001

H3R antagonists





Conclusion

Surprisingly, the H3R antagonist/inverse agonist (A331440 and thioperamide) and the H3R agonists (immepip and imetit) produce a statistically significant enhancement of the sedative effects induced by ethanol. Future investigations are needed to better understand the mechanism(s) underlying these unexpected results, that might be related to unspecific effects of these drugs.