Ethanol-induced behaviours in mice genetically lacking the MCH_1 receptor.

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Introduction

The melanin-concentrating hormone (MCH) and its receptors MCH_1 ($MCHR_1$) are largely involved in the regulation of feeding behaviours and in the energy balance/homeostasis. Additionally, MCH could also display modulatory actions on the effects of addictive drugs. Recently, it has been shown that mice genetically lacking the MCH1 receptor ($MCHR_1$ KO) consume more alcohol than the wild-type (WT) and the heterogeneous mice (Ducan et al.,2007).

The **aim** of this study was to **investigate the possible modulations of ethanol-induced sedation, locomotion and aversion by the depletion of $MCHR_1$ in mice.**

Methods

Animals:
351 Female MCHR1-KO and -WT mice were used for the experiments. Mice were derived by heterozygous intercross and had a mixed 129SvJxC57Bl/6 background (see Lakaye et *al., 2004*).

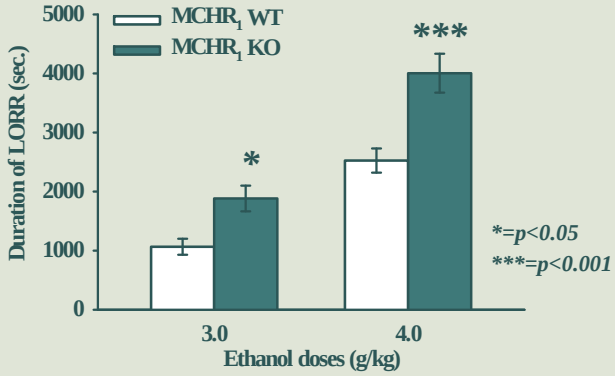
Sedation:
To assess the sedative effects of ethanol, 3.0 g/kg or 4.0 g/kg of ethanol were injected and the duration of the loss of righting reflex (LORR) was measured.

Locomotion:
Locomotion induced by the injection of various ethanol doses (0.0 to 2.5 g/kg) was measured in white openfields (40x40cm) using a videotracking system (Viewpoint, France).

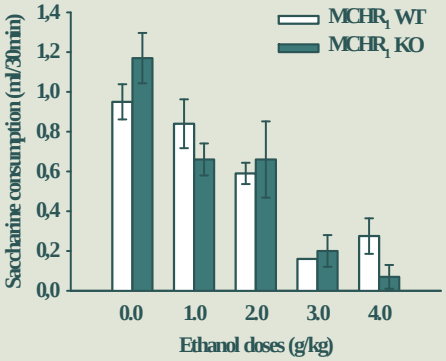
Aversion:
To assess the aversive effects induced by ethanol, we used a classical protocol: the conditioned taste aversion. On alternate days, mice were presented with a saccharin solution (pairing days) and with tap water (non-pairing days) for 30 min. On pairing days, mice were allowed to drink a saccharin solution for 30 min in test cage. Immediately after the drinking session, the mice were i.p. injected with ethanol (0, 1.0, 2.0, 3.0 or 4.0 g/kg). Such a conditioning procedure allowed the mice to associate the novel taste of the saccharin solution with the effects of a specific ethanol dose. The consumption of saccharine on the 4th pairing day is used to evaluate the aversive effect of ethanol.

Results

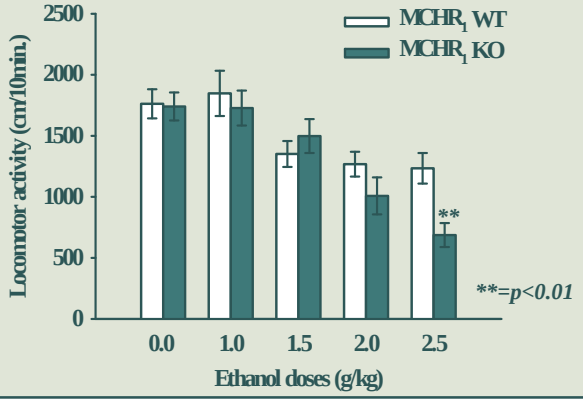
Loss of righting reflex

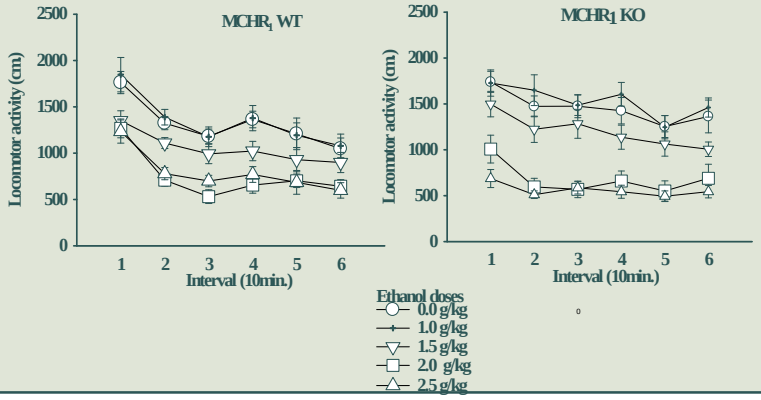


Conditioned taste aversion



Ethanol-induced locomotion





Conclusion:

- **These experiments clearly show an increased ataxic and sedative effects of ethanol in MCHR1 KO;**
- **However, in this study, MCHR1 do not seem to be implicated in the aversive effects of alcohol.**