Glucocorticoid Receptor Regulation of Binge-like Ethanol Intake
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Abstract
Glucocorticoid receptors (GR) have emerged as an important target for alcohol abuse. Dependence-induced escalations in alcohol intake can be prevented by administration of GR antagonists, but these same compounds have had little effect in non-dependent animals. Here, we investigated the role of GR in binge-like ethanol intake in the High Drinking in the Dark (HDID-1) line of mice and their founder line, HS/Npt.

Methods & Results

Drinking in the Dark (DID): HDID-1 or HS/Npt mice (M+F) were given a single bottle 3 hours after lights out containing either 20% ethanol, water, or 8.5 mM saccharin. Animals received food and water ad libitum outside limited access testing.

Ethanol Conditioned Taste Aversion (CTA): HDID-1 mice (M+F) were tested for development of CTA to a novel NaCl drinking solution following paired injections with (a) saline or 2 g/kg EtOH, and (b) vehicle or mifepristone (25 or 50 mg/kg).

Pathway of Interest

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Conclusions
- Mifepristone and CORT113176 reduced non-dependent binge-like ethanol intake in HDID-1 mice
- These are the first data to suggest GR antagonism could reduce non-dependent excessive alcohol intake, and suggest a role for GR activity in the genetic susceptibility to binge-like drinking
- CORT113176 did not reduce binge-like ethanol intake in the founder line, HS/Npt
- These, and the above data, suggest that genetic changes elicited by selection for high BECs in HDID-1 mice have led to a sensitized response to GR antagonism
- Mifepristone did not enhance ethanol CTA or CPA
- HDID-1 mice show an attenuated response to GR antagonism could reduce non-dependent binge-like ethanol intake and blood ethanol concentrations (BECs) in the HDID-1 mice. GR antagonism did not reduce ethanol intake or BECs in the HS/Npt mice, suggesting that GR may have become sensitized through the selection process.

We further investigated whether GR antagonism was altering ethanol’s aversive effects by testing HDID-1 mice in ethanol conditioned taste (CTA) and place aversion tasks (CPA). Although HDID-1 mice continued to show an attenuated aversive response to a moderate dose of ethanol (2 g/kg), as demonstrated previously, GR antagonism did not alter ethanol CTA or CPA.