

Influence of b-Endorphin on Alcohol Mediated Reinforcement

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Alcohol (EtOH) alters opioid systems

- Acute EtOH increases opioid gene transcription, biosynthesis and release (both *in vitro* and *in vivo*)
- Chronic EtOH decreases opioid gene transcription, biosynthesis and release
- Possible increase in responsiveness of opioids to EtOH in animals and people prone to high EtOH consumption

Gianoulakis et al., 1995

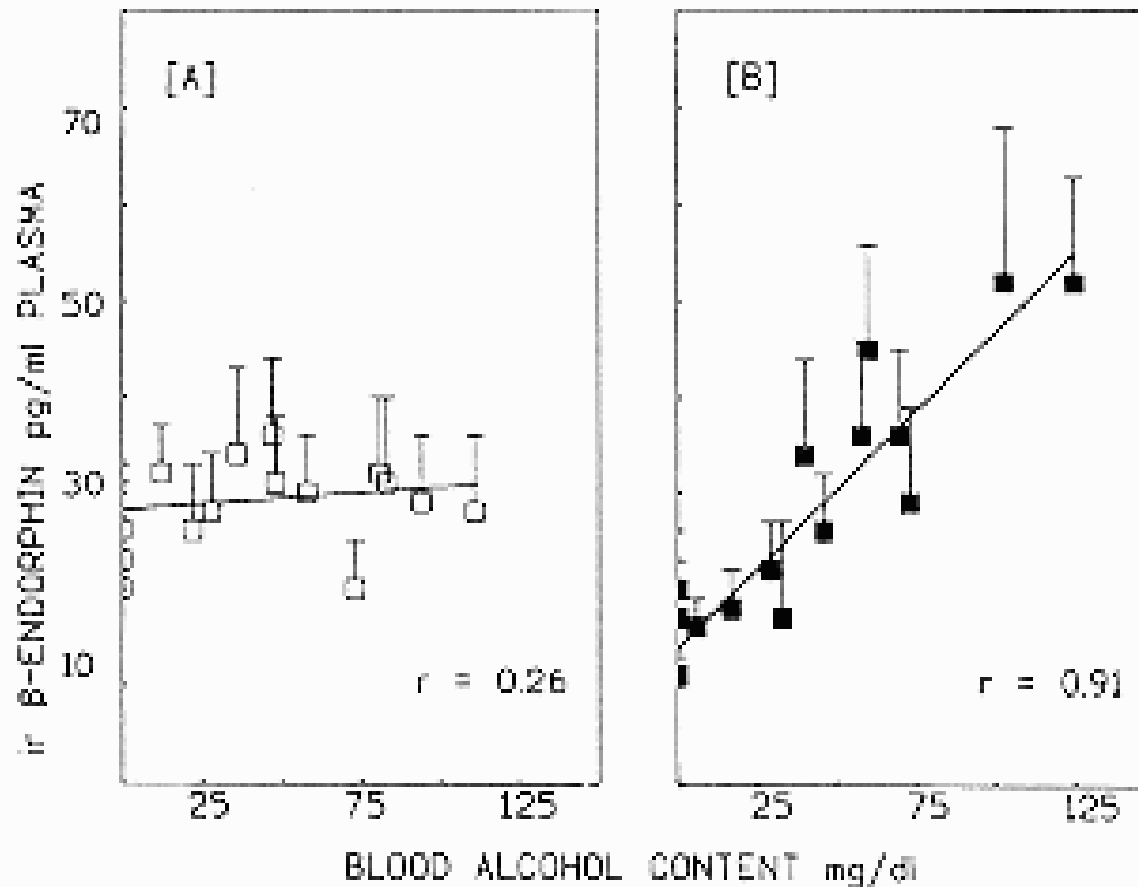
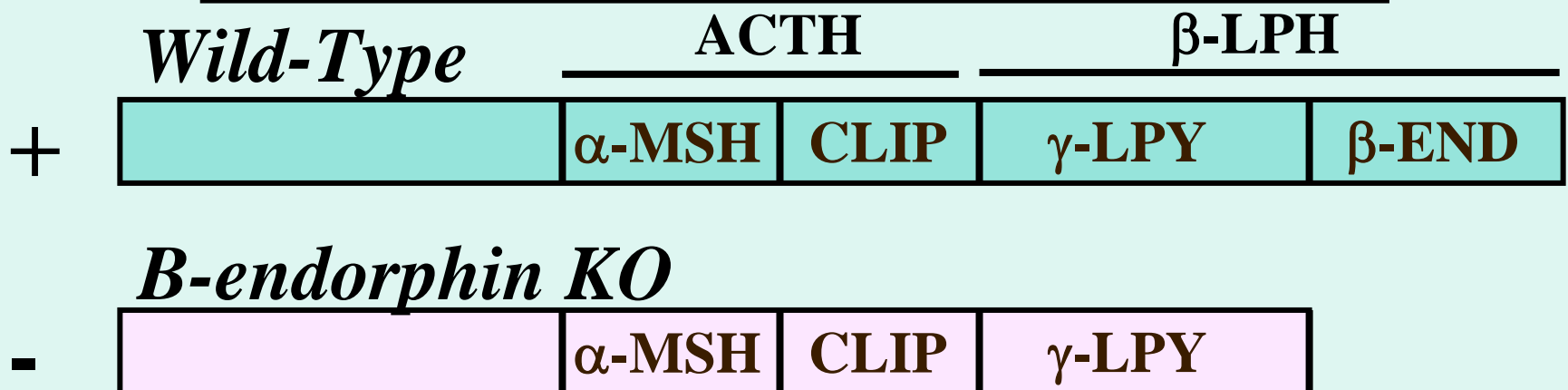
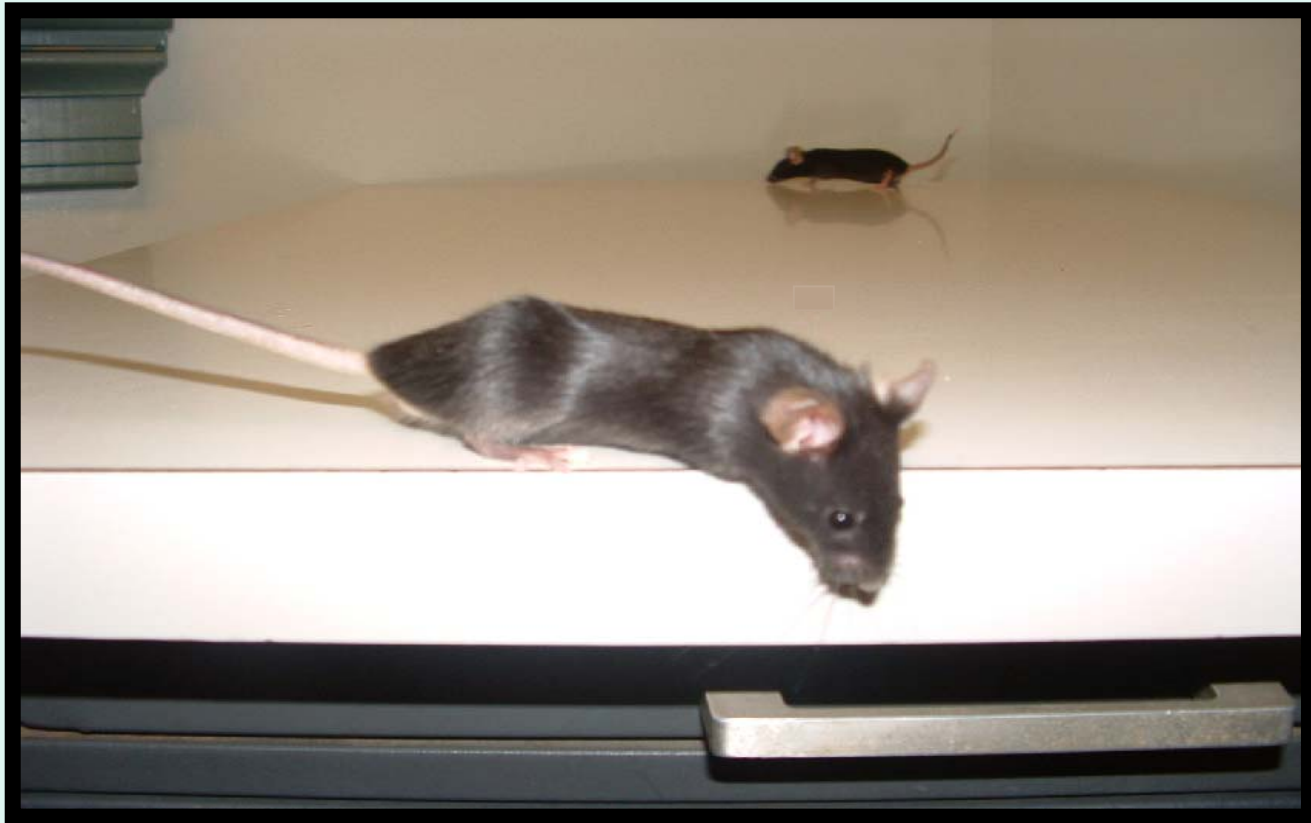
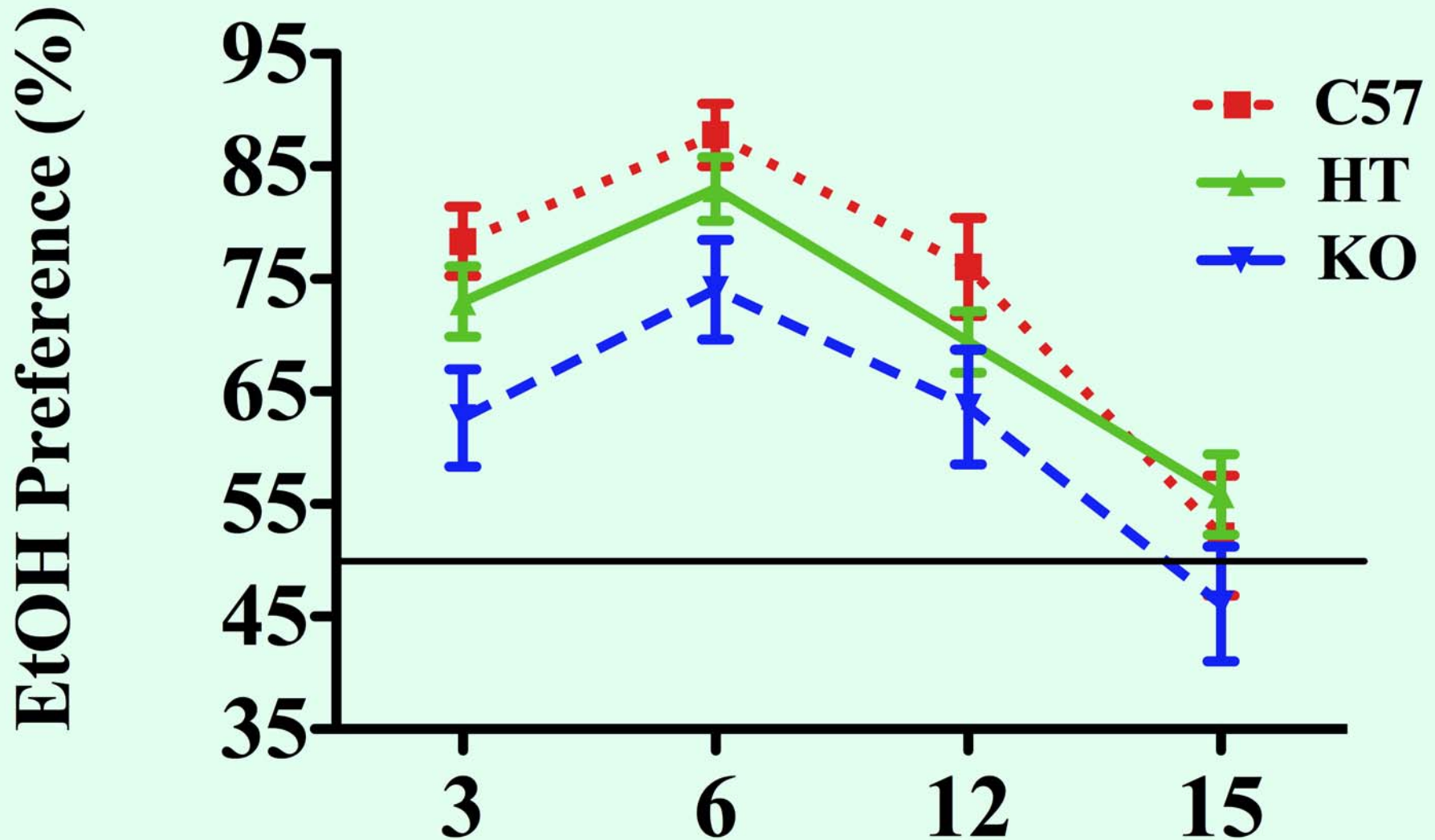


Figure 4. Linear regression analysis of the plasma β -endorphin content vs. the blood alcohol content for the low-risk (A) and the high-risk (B) subjects, as defined in figure 3.

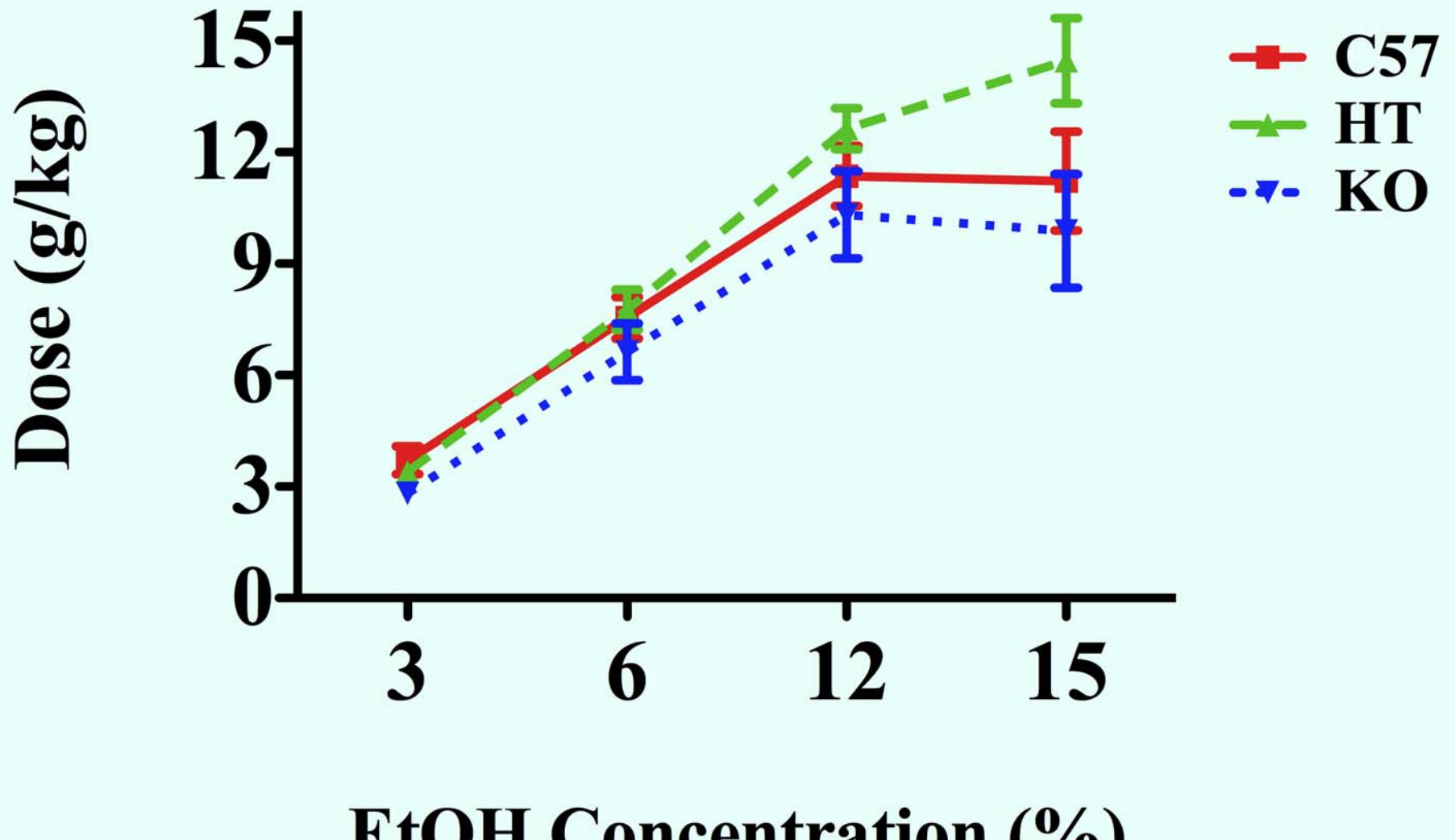
β -endorphin deficiency on C57BL/6J background



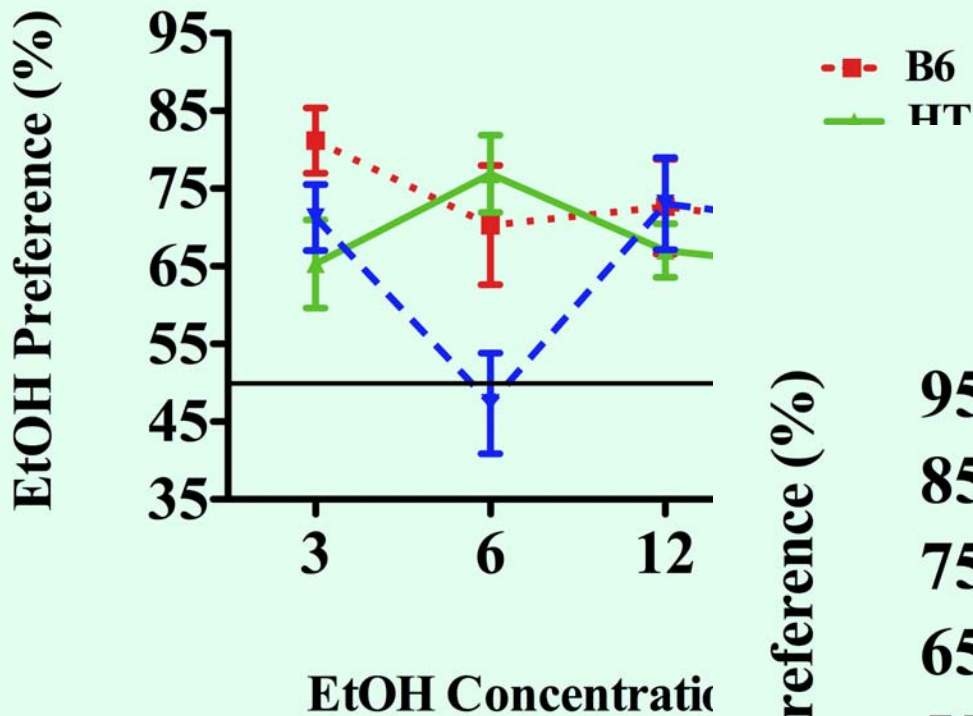
Average Preference (%)



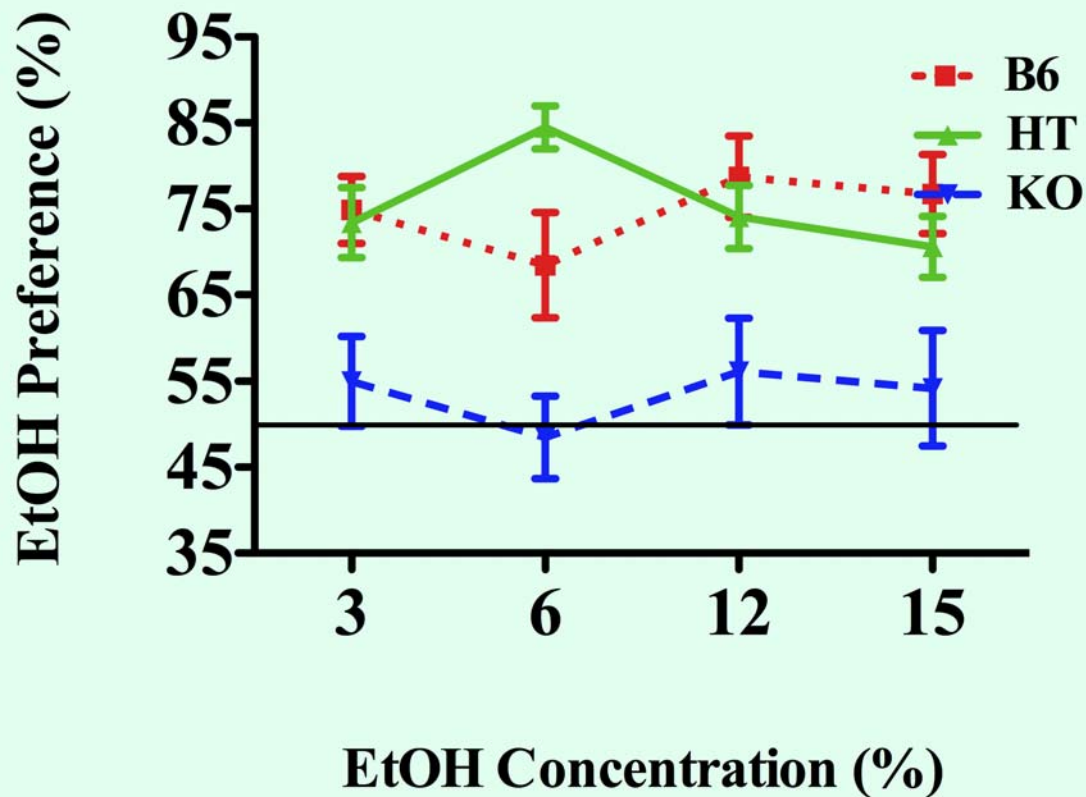
Average Dose



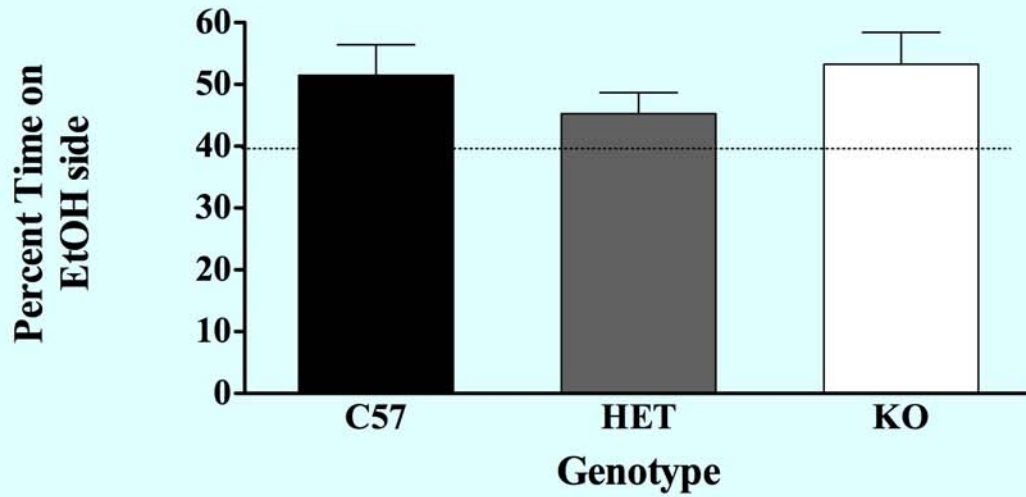
Female Average Preference (%)



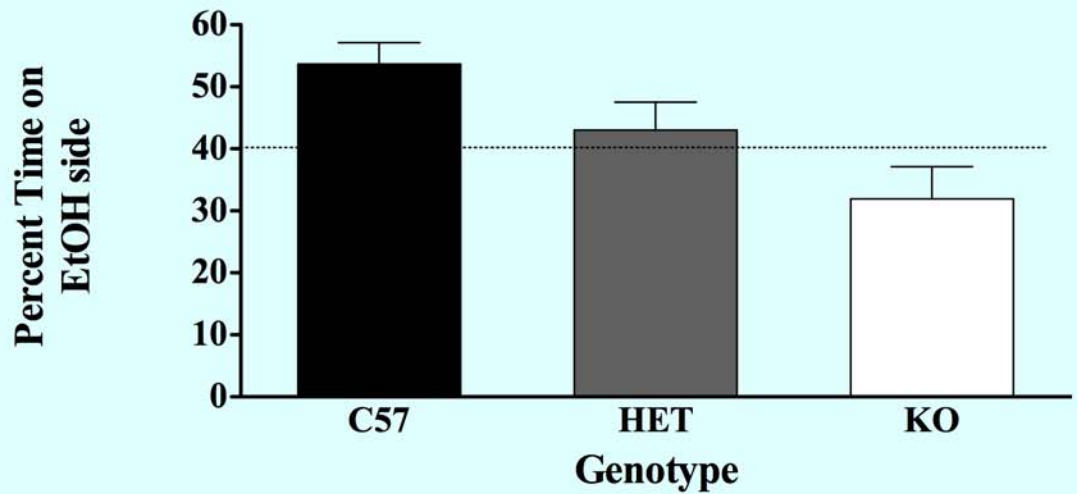
Male Average Preference (%)



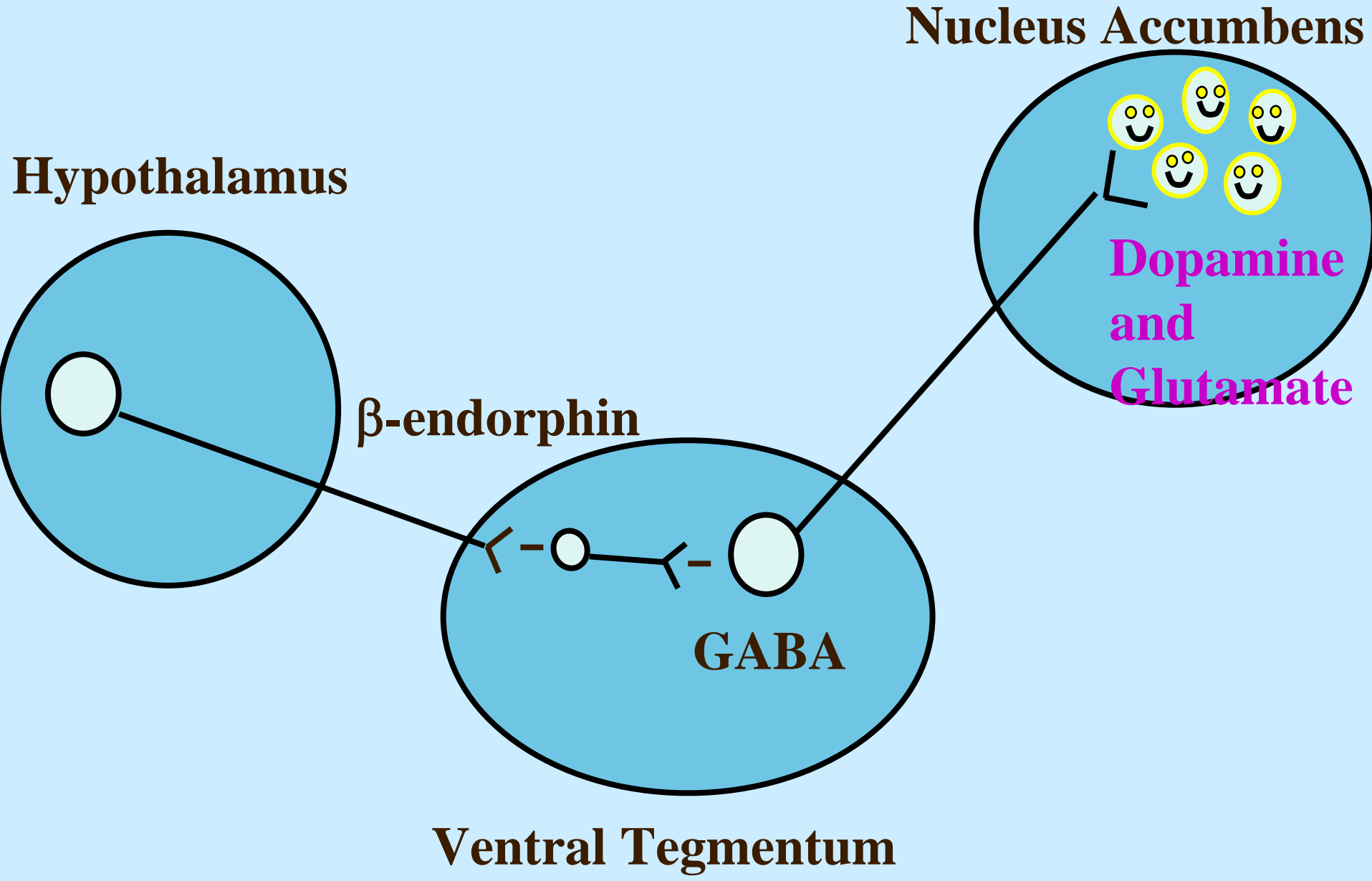
Females



Males



β -endorphin and pleasure



Direct assessment of Reward Hypothesis

- Using in vivo microdialysis to investigate neurochemical differences in b-endorphin deficient mice
- Glutamate and Dopamine levels in nucleus accumbens

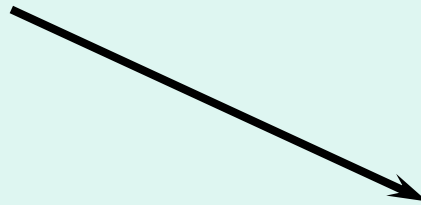
**EtOH
Drinking**

B-endorphin?



Positive Reinforcement

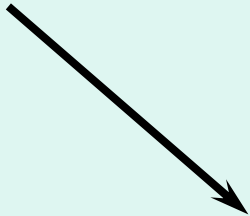
B-endorphin?



Negative Reinforcement

How stress axis moderates
EtOH response
/ liability for abuse and dependence

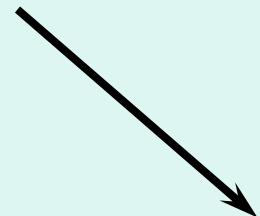
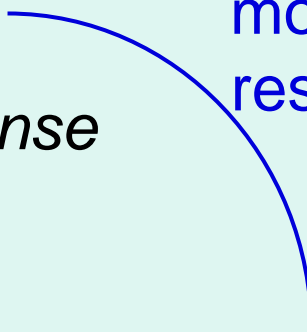
b-endorphin



Acute EtOH

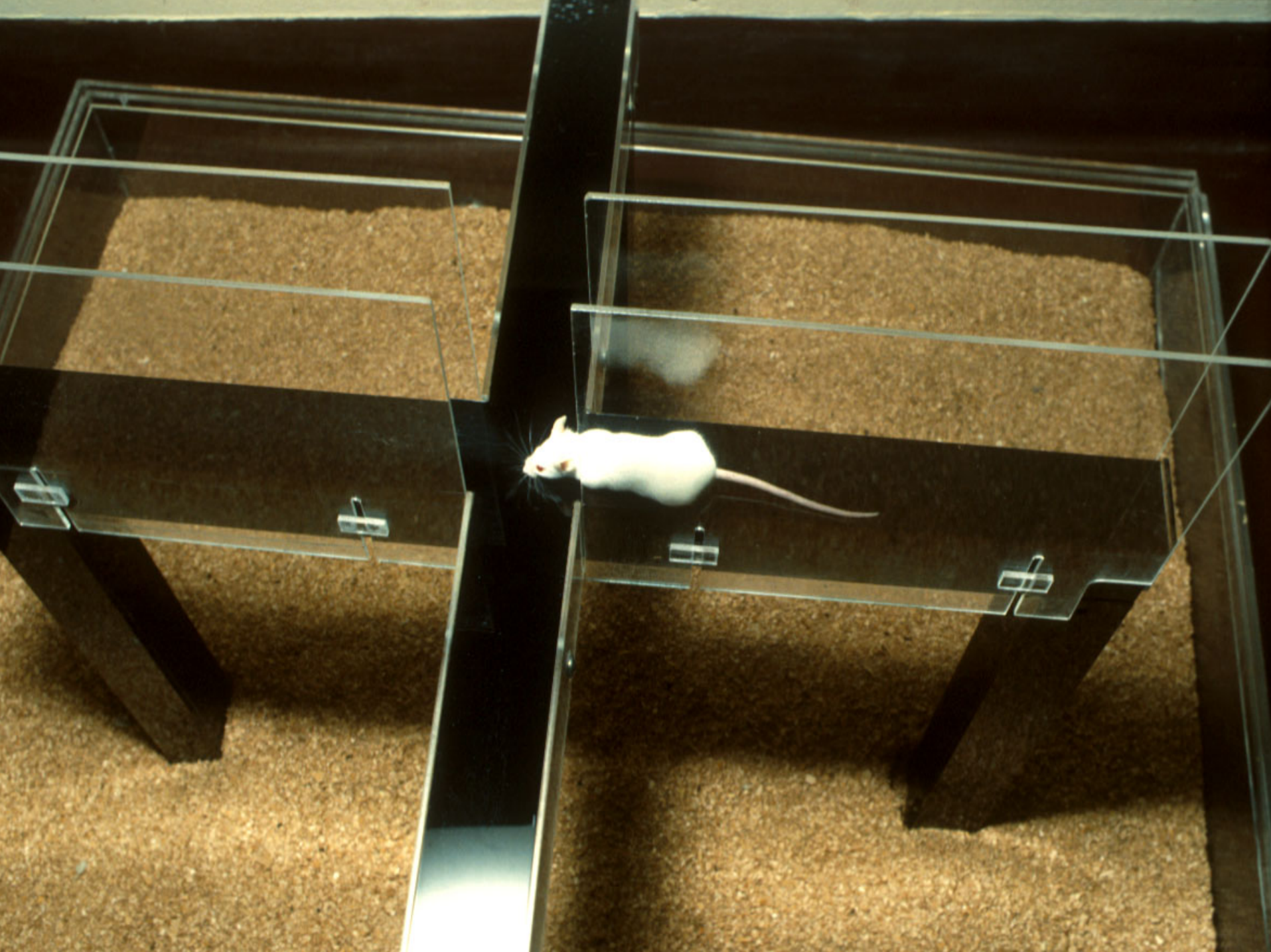
Induces stress response

How EtOH
moderates stress
response



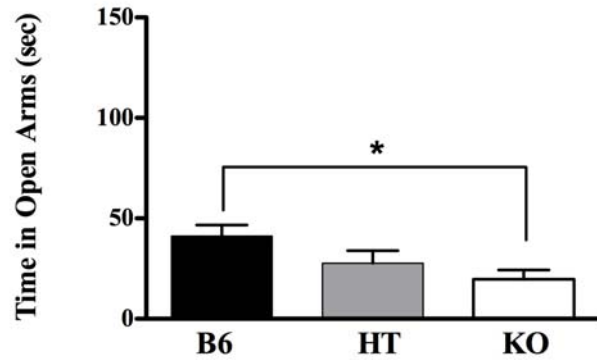
Chronic EtOH

*Downregulated stress response;
hyperactivity upon withdrawal*

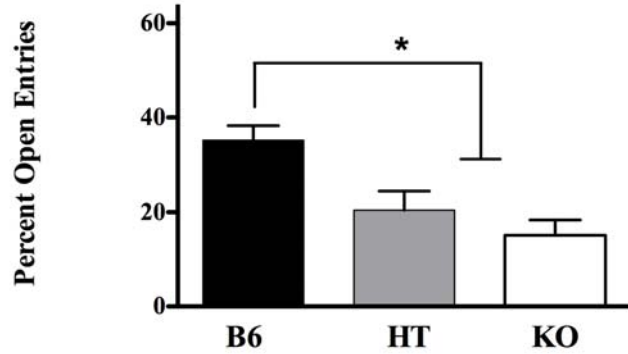


Plus Maze

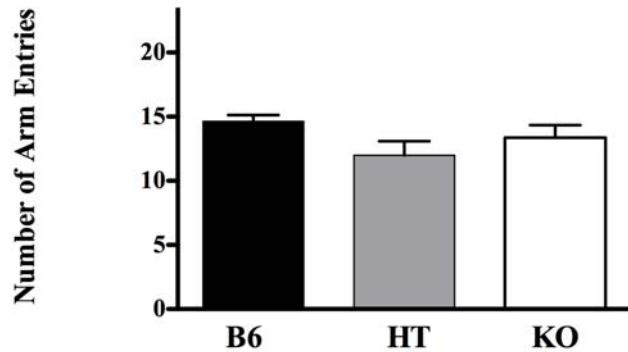
a.



b.

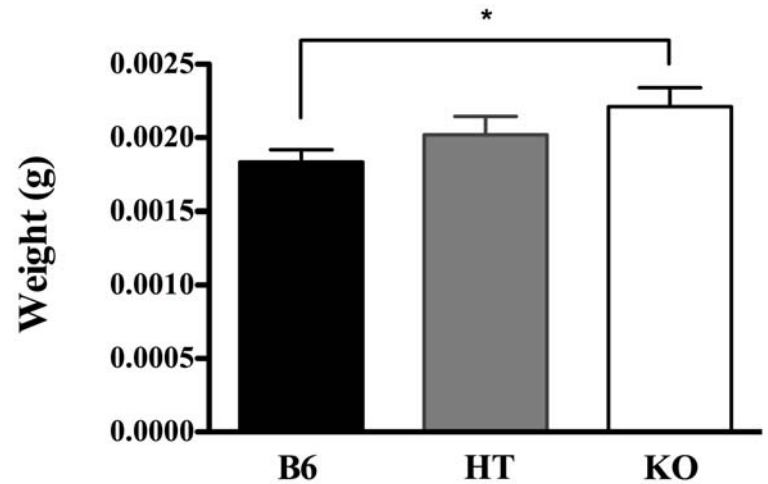


c.



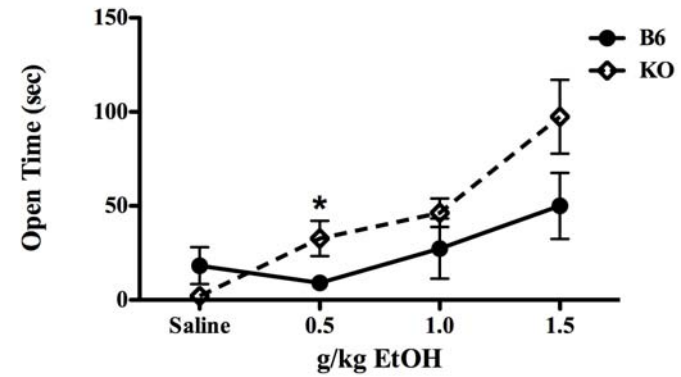
Low b-endorphin =
high stress/anxiety

Adrenal Weights

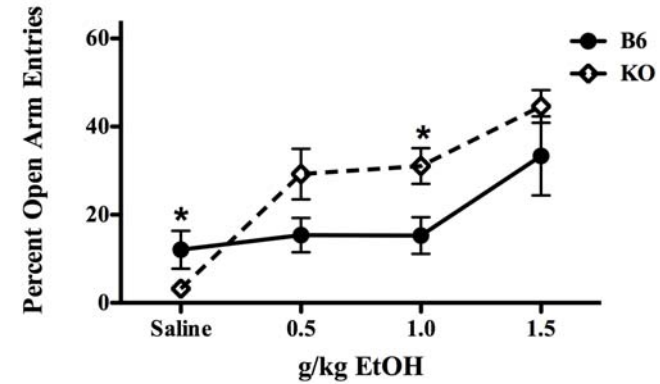


Absent b-endorphin increases EtOH - mediated decrease in anxious behavior

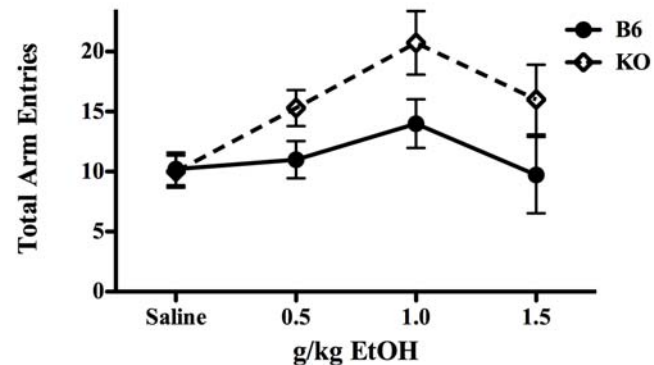
a.



b.



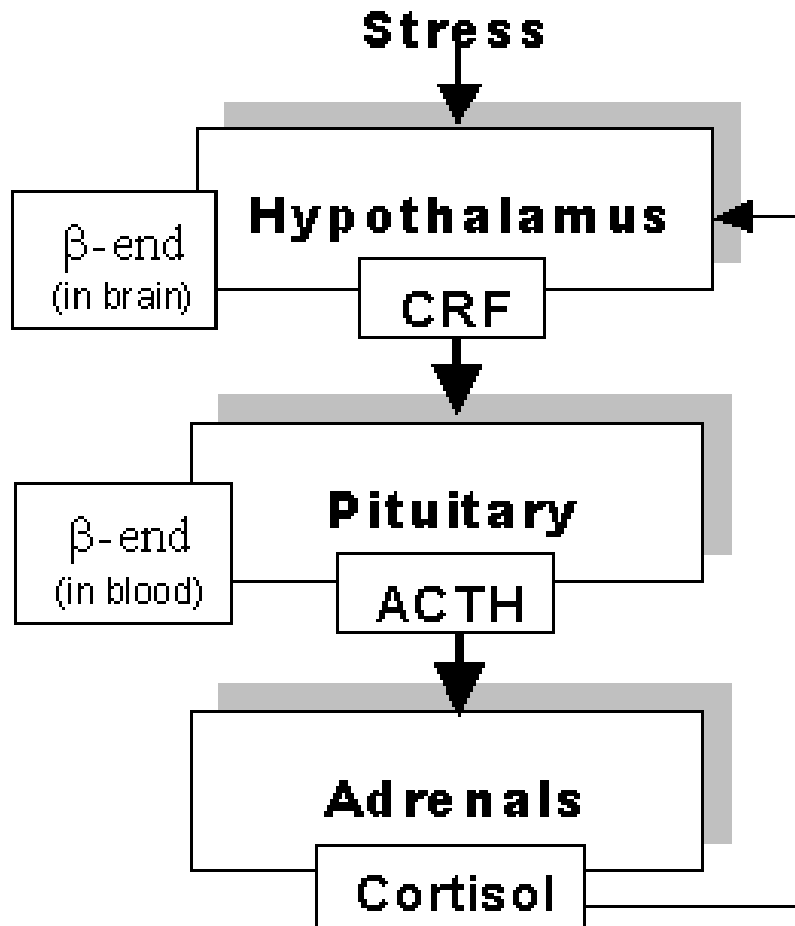
c.



Stress, b-endorphin and EtOH

- Does b-endorphin modulate the impact of stress on EtOH?
- *Preliminary studies indicate that Stress appears to enhance conditioned place effects of EtOH in a b-endorphin-dependent manner.*

HPA Axis Response



CRF - corticotropin-releasing factor;
ACTH - adrenocorticotropic hormone;
β-end - beta-endorphin

- ACTH and β -Endorphin are released by the activation of the same precursor molecule (POMC)
- Hypothesis: β -endorphin may mediate the effects of stress

Acknowledgements

Students:

Stephani Allen, Jess Bartels, Greg Cloonan, **Lori Jones**, Amanda Lee, **Ashley Holloway** (USC, Orangeburg) Carmen Sanchez, **Chris Smith**, Sidney Williams

NIH

P20 RR-016461 / INBRE

AA13259 (through the INIA Stress consortium)

AA13641