Washington University School of Medicine
Digital Commons@Becker

Posters

2004: Alcoholism and the Latest Genetics and Neuroscience Findings

2004

Increased ethanol drinking by rIIâ knockout mice: Assessment of genetic background and testing procedures

Jon R. Fee
University of North Carolina at Chapel Hill

Dennis R. Sparta
University of North Carolina at Chapel Hill

Mitchell J. Picker
University of North Carolina at Chapel Hill

Todd E. Thiele
University of North Carolina at Chapel Hill

Follow this and additional works at: http://digitalcommons.wustl.edu/guzeposter2004

Part of the Medicine and Health Sciences Commons

Recommended Citation
Fee, Jon R.; Sparta, Dennis R.; Picker, Mitchell J.; and Thiele, Todd E., "Increased ethanol drinking by rIIâ knockout mice: Assessment of genetic background and testing procedures" (2004). *Posters*. Paper 2 Samuel B. Guze Symposium on Alcoholism.
http://digitalcommons.wustl.edu/guzeposter2004/2

This Poster is brought to you for free and open access by the 2004: Alcoholism and the Latest Genetics and Neuroscience Findings at Digital Commons@Becker. It has been accepted for inclusion in Posters by an authorized administrator of Digital Commons@Becker. For more information, please contact engeszer@wustl.edu.

Increased Ethanol Drinking by RIIβ Knockout Mice: Assessment of Genetic Background and Testing Procedures

Jon R. Fee[1*], Dennis R. Sparta[1], Mitchell J. Picker[1] and Todd E. Thiele[1,2]

[1]Department of Psychology and [2]The Bowles Center for Alcohol Studies, University of North Carolina, Chapel Hill, NC 27599-3270

*address correspondence to JonFee@unc.edu

UNC SCHOOL OF MEDICINE
BOWLES CENTER FOR ALCOHOL STUDIES

Introduction

Mice lacking the regulatory subunit RIIbeta (RIIβ) of protein kinase A (PKA) maintained on a mixed 129/SvJ x C57BL/6 background have been shown to consume more ethanol than littermate wildtype controls (Thiele et al., (2000). J. Neuroscience 20: RC75 1-6).

Expression of phenotypes, including altered voluntary consumption of ethanol, can depend on the genetic background of the knockout model.

Thus, it was important to determine if RIIβ knockout mice show increased consumption of ethanol when backcrossed to alternate background strains.

Methods

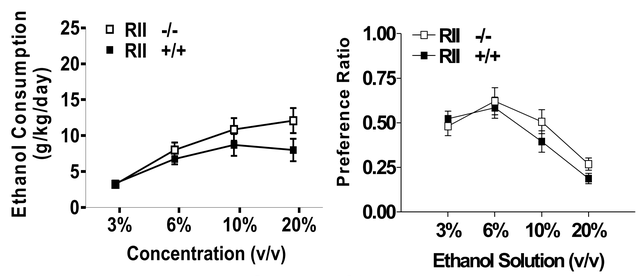
Subjects: RIIβ -/- mice were created through the disruption of the RIIβ gene by homologous recombination in embryonic stem cells from 129/SvJ mice (Brandon et al., 1998). Chimeras were bred with C57BL/6 mice to obtain heterozygotes (50% 129/SvJ x 50% C57BL/6). These heterozygotes were backcrossed with C57BL/6 mice to yield RIIβ+/- mice on an ~100% C57BL/6 genetic background. For some experiments described here, non-littermate RIIβ+/- mice on the 100% C57BL/6 background were bred, resulting in RIIβ-/- and RIIβ+/+ F2 littermate mice. Additional experiments involved RIIβ-/- and RIIβ+/+ F2 littermate mice on a 50% 129/SvEv x 50% C57BL/6 background that were created by crossing the RIIβ-/- mice with wild-type 129/SvEv mice. The genetic status of all mice was determined using polymerase chain reaction (PCR) procedures. Animals weighed approximately 20 g, were 3 to 6 months of age at the beginning of experiments, and were individually housed in polypropylene cages with corncob bedding. Mice had ad libitum access to water and standard rodent chow (Tekland, Madison, WI). The colony room was maintained at approximately 22° C with a 12h:12h light:dark cycle with lights off at 3:00 pm. All procedures used in the present study were in compliance with the National Institute of Health guidelines, and the protocols were approved by the University of North Carolina Institutional Animal Care and Use Committee.

Steep Ramping Procedure: Initial ethanol testing was done using a two bottle choice paradigm in which mice from each genotype were presented with one bottle containing a 3% ethanol and tap water solution and a second bottle contained only tap water. Every eight days, the ethanol concentration was increased to 6, 10, and finally 20%. The test concluded after 32 days.

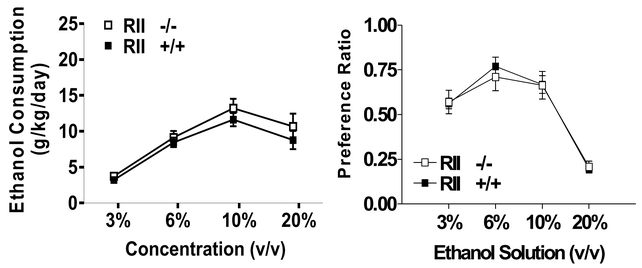
Gradual Ramping Procedure: A second group of ethanol naïve mice from each genotype were run through a two bottle choice paradigm in which ethanol concentrations were increased more gradually. However, the same range of concentrations was tested over the same time period. Every 4 days, ethanol concentrations were increased from 3, 5, 8, 10, 13, 15, 18, and 20%.

Steep Ramping Consumption and Preference Ratio

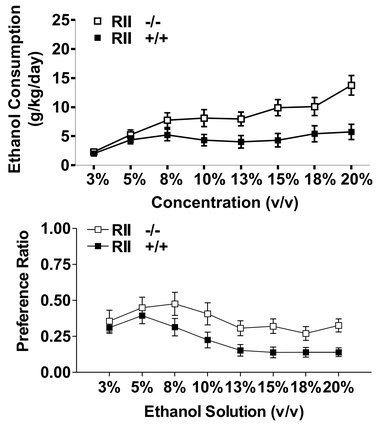
129/SvEv x C57BL/6



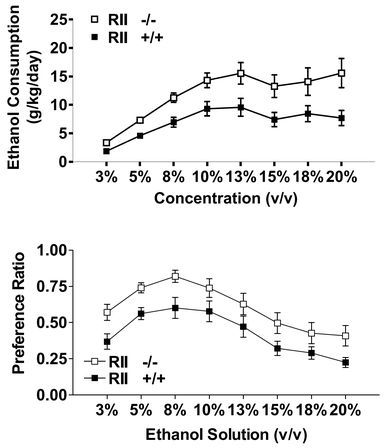
C57BL/6



129/SvEv x C57BL/6 Gradual Ramping Consumption and Preference Ratio



C57BL/6 Gradual Ramping Consumption and Preference Ratio



Conclusions

The gradual ramping procedure resulted in significant genotype differences with RIIβ -/- mice consuming significantly more ethanol than wildtype littermate controls.

Both male and female mice were tested and a genotype by sex interaction was not observed.

Increased consumption in RIIβ knockout mice was not genetic background dependent. We are currently backcrossing the mutation to a third genetic background (129/SvEv) to further strengthen this conclusion.

These data indicate that a gradual ramping of increasing ethanol concentrations may be a more sensitive measure for detecting altered ethanol drinking in mice.

Funding

Supported by NIH grants AA00258, AA13573, DA10277, and a Junior Faculty Development Award from the University of North Carolina