Development of individual alcohol inhalation chambers for mice: validation in a model of prenatal alcohol.

Abstract

BACKGROUND:

The purpose of this work was first to develop a system of individual chambers through which controlled delivery of alcohol vapors allows us to target specific blood alcohol levels (BALs) in mice without requiring the administration of an alcohol dehydrogenase inhibitor. As a proof of concept, we demonstrated that this new system could be used to expose pregnant BALB/c or C57BL/6 mice to alcohol and that the hypothalamic-pituitary-adrenal (HPA) axis of their mature offspring exhibited the well-known hyperactivity that has been previously documented in rats.

METHODS:

A first series of experiments was designed to establish the parameters that resulted in specific BALs in nonpregnant adult male and female BALB/c as well as C57BL/6 mice that were exposed to various alcohol flow rates. Using information gathered from these experiments, we then chose a regimen of 6 hr of daily vapor exposure in pregnant mice to determine whether this regimen would alter the HPA axis activity of their mature offspring. Control dams were maintained in similar chambers but without alcohol. We first used control mice to assess plasma ACTH levels as a function of shock intensity as well as total duration of the shock session. The most suitable protocol was then used to measure shock-induced ACTH release in 2-month-old male and female offspring that were exposed to alcohol prenatally or not.

RESULTS:

BALs increased as a function of the alcohol flow rates and remained within an acceptable range of homogeneity, consistency, and reproducibility over the desired periods of time. There were no sex differences in BALs while vapors were delivered. However, there was a strain difference in that BALB/c mice displayed slightly higher BALs than C57BL/6. Female mice also exhibited a slightly more pronounced decrease in BALs, compared with male mice, once removed from the drug. Measurement of plasma ACTH levels as a function of the intensity and duration of the shock sessions indicated that 0.3 mA intensity, 1-sec duration shocks at the rate of 2 shocks/min for 20 min provided the most reliable protocol. We then used the alcohol model in pregnant mice. Alcohol exposure did not interfere with maternal weights during gestation. When offspring were tested at 8 to 9 weeks of age, male and female BALB/c as well as female C57BL/6 mice that were exposed to alcohol vapors prenatally exhibited significantly higher shock-induced plasma ACTH levels, compared with controls of the same strain.

CONCLUSIONS:

Collectively, our results indicate that the individual alcohol chamber system that we have developed offers a reliable means of exposing mice to alcohol so that they reach predetermined BALs in the absence of the pharmacological manipulations often used to influence alcohol metabolism in this species. This system, which is compatible with normal weight gains, was used to provide evidence that as previously demonstrated in rats, adult murine offspring of alcohol-treated dams exhibit a hyperactive HPA axis. The development of protocols for use in mice offers the possibility of investigating the influence of alcohol in mutant animals with manipulations of specific genes of interest.