Repeated Daily Drinking-in-the-Dark Results in Inflexible Ethanol Drinking in C57BL/6J Mice

**Michel A. Companion**, Stephen L. Boehm II
Indiana Alcohol Research Center, Department of Psychology, IUPUI School of Science

We recently demonstrated that repeated daily binge ethanol (EtOH) intake (Drinking-in-the-Dark; DID) alters the pattern of subsequent binge drinking, suggesting neuroadaptation as a consequence of repeated binge drinking. The current objective was to determine whether repeated binge drinking behavior using DID procedures produces a compulsive pattern of drinking. We took advantage of a paradigm in which the aversive stimulus quinine is used to adulterate the EtOH solution after a history of EtOH drinking. Using this approach, Lesscher et al. (2010) demonstrated that C57BL/6J (B6) mice develop inflexible drinking after repeated binge-like EtOH drinking; that is, mice with longer drinking histories become insensitive to the quinine addition, “compulsively” consuming the EtOH solution despite the aversive stimulus. Seventy male B6 mice (PND 60) from Jackson Laboratory were randomly assigned to one of seven fluid consumption groups using DID procedures (daily 2hr EtOH access, 3 hrs into the dark cycle). The first group received access to a 20% (v/v) EtOH in tap water for 6 weeks. The second group also received access to the EtOH solution for six weeks, but with the addition of a low concentration of quinine (0.35mM) that produces minimal avoidance in naïve B6 mice in the sixth week. The third group was treated similarly; however, on the sixth week a higher concentration of quinine (0.45mM) that produces clear avoidance in naïve B6 mice was added to the EtOH solution. The fourth and fifth groups received access to the EtOH solution two weeks prior to adulteration with the low or high quinine concentration, respectively, for one week. Groups six and seven were allowed access to the EtOH solution for one week before the lower or higher concentrations of quinine were added, respectively, for one week. Two naïve groups with no previous DID exposure were also presented with low or high concentrations of quinine adulterated EtOH solution for comparison. We predicted that daily binge EtOH drinking for two and five weeks (but not one week) would result in resistance to the aversive quinine (inflexible drinking). However, results showed that even one week of DID produced inflexible drinking. Future studies are planned to examine binge drinking durations within the first week of DID to determine precisely when this shift to more compulsive drinking occurs. This work was supported by NIH grants AA007611 (SLB) and GM109432 (MAC).

Mentor: Stephen L. Boehm II, Psychology Department, IUPUI School of Science. Indianapolis, IN