Available online at www.sciencedirect.com
SCIENCE DIRECT
Pharmacology, Biochemistry and Behavior 83 (2006) 35 – 46
PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR
www.elsevier.com/locate/pharmbiochembeh

Daily patterns of ethanol drinking in peri-adolescent and adult alcohol-preferring (P) rats

Richard L. Bell [a,*], Zachary A. Rodd [a], Helen J.K. Sable [a], Jonathon A. Schultz [a], Cathleen C. Hsu [a], Lawrence Lumeng [b,c], James M. Murphy [a,d], William J. McBride [a,c]

[a] *Department of Psychiatry, Institute of Psychiatric Research, Indiana University School of Medicine, Indianapolis, IN 46202 USA*
[b] *Department of Medicine, Indiana University School of Medicine, Indianapolis, IN 46202 USA*
[c] *Department of Biochemistry, Indiana University School of Medicine, Indianapolis, IN 46202 USA*
[d] *Department of Psychology, Purdue School of Science, Indiana University Purdue University at Indianapolis, Indianapolis, IN 46202 USA*

Received 21 May 2005; received in revised form 2 December 2005; accepted 6 December 2005
Available online 26 January 2006

Abstract

Alcohol abuse among adolescents continues to be a major health problem for our society. Our laboratory has used the peri-adolescent alcohol-preferring, P, rat as an animal model of adolescent alcohol abuse. Even though peri-adolescent P rats consume more alcohol (g/kg/day) than their adult counterparts, it is uncertain whether their drinking is sufficiently aggregated to result in measurable blood ethanol concentrations (BECs). The objectives of this study were to examine daily alcohol drinking patterns of adolescent and adult, male and female P rats, and to determine whether alcohol drinking episodes were sufficiently aggregated to result in meaningful BECs. Male and female P rats were given 30 days of 24 h free-choice access to alcohol (15%, *v*/*v*) and water, with ad lib access to food, starting at the beginning of adolescence (PND 30) or adulthood (PND 90). Water and alcohol drinking patterns were monitored 22 h/day with a "lickometer" set-up. The results indicated that (a) peri-adolescent P rats consumed more water and total fluids than adult P rats, (b) female P rats consumed more water and total fluids than male P rats, (c) there were differences in alcohol, and water, licking patterns between peri-adolescent and adult and female and male P rats, (d) individual licking patterns revealed that alcohol was consumed in bouts often exceeding the amount required to self-administer 1 g/kg of alcohol, and (e) BECs at the end of the dark cycle, on the 30th day of alcohol access, averaged 50 mg%, with alcohol intakes during the last 1 to 2 h averaging 1.2 g/kg. Overall, these findings indicate that alcohol drinking patterns differ across the age and sex of P rats. This suggests that the effectiveness of treatments for reducing excessive alcohol intake may vary depending upon the age and/or sex of the subjects being tested.

Keywords: Adolescence; Young adult; Juvenile; Alcohol-preferring rats; Alcohol-drinking

1. Introduction

Today's youth are initiating alcohol use earlier and experiencing more alcohol-related problems than ever before (Miller et al., 2001; Winters, 2001), and this is true for both men and women (Kandel et al., 1997; Nelson et al., 1998). Recent estimates indicate that 80% of high school seniors have consumed alcohol and half of these initiated drinking before the eighth grade (Johnston et al., 1999), with early onset of alcohol use serving as a strong predictor of future alcohol dependence (Grant and Dawson, 1997; Hawkins et al., 1997). Binge drinking during high school and college is becoming more prevalent and is also a strong predictor of future alcohol-related problems in both men and women (Presley et al., 1994; Wechsler et al., 2000). Pattern of drinking (binge drinking, which is characterized by periods of large volumes of ethanol intake per day separated by periods of abstinence, versus constant ethanol consumption, which is generally characterized by lower volumes of intake per day) and total volume consumed are important diagnostic criteria for the onset of alcoholism in adult individuals as well (e.g., Heather et al., 1993; Lancaster, 1994). Additionally, these criteria have been used to develop different typologies and/or drinking profiles for alcoholics (e.g., Babor et al., 1992; Cloninger, 1987; Conrod et al., 2000; Epstein et al., 1995; Prelipceanu and

* Corresponding author. Tel.: +1 317 278 4629; fax: +1 317 274 1365.
E-mail address: ribell@iupui.edu (R.L. Bell).

0091-3057/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.pbb.2005.12.004

Mihailescu, 2005; Windle and Scheidt, 2004; Zucker, 1987). Furthermore, in some cases, the effectiveness of a particular treatment appears to depend upon where an individual ranks on the continuum of a typology (e.g., Cherpitel et al., 2004; Dundon et al., 2004; Epstein et al., 1995; Johnson et al., 2003). Therefore, both age-of-onset and pattern of drinking are factors that have predictive validity for a life-time diagnosis of alcoholism or alcohol abuse and, in some cases, the effectiveness of the treatment for the same. The importance of investigating patterns of ethanol intake is also supported by research with rodents. Recent research from our laboratory has indicated that different selectively bred, high alcohol-consuming lines of rats may display different "types" of drinking (e.g., binge-like versus more continuous-like) under free-choice, home-cage conditions (Bell et al., 2004), which has also been found when selectively bred, high alcohol-consuming rats were tested using operant procedures (Files et al., 1998; Samson et al., 1998). In addition, it appears that examination of ethanol intake patterns, across a 24 h period, may reveal the role of endogenous factors (e.g., hormones and/or neurotransmitters) that mediate ethanol self-administration behavior, which might not be evident from records of daily intake alone (c.f., Samson, 2000).

Given the prevalence of alcohol abuse during adolescence, a need for animal models of excessive alcohol drinking during adolescence has been indicated (Spear, 2000; Witt, 1994). Peri-adolescent pups of selectively bred high alcohol-consuming lines of rats (e.g., alcohol-preferring, P, rats) have been proposed as one animal model of adolescent alcohol abuse (c.f., McBride et al., 2005; McKinzie et al., 1999). This stems from the fact that the P line of rat successfully meets criteria (c.f., Bell et al., 2005; McBride and Li, 1998; Murphy et al., 2002) proposed for a valid animal model of alcoholism (Cicero, 1979; Lester and Freed, 1973). Briefly, these criteria are as follows: 1) the animal should orally self-administer ethanol; 2) the amount of ethanol consumed should result in pharmacologically relevant blood ethanol levels; 3) ethanol should be consumed for its post-ingestive pharmacological effects, and not strictly for its caloric value or taste; 4) ethanol should be positively reinforcing, in other words, the animals must be willing to work for ethanol; 5) chronic ethanol consumption should lead to the expression of metabolic and functional tolerance; and 6) chronic consumption of ethanol should lead to dependence, as indicated by withdrawal symptoms after access to ethanol is terminated (Cicero, 1979; Lester and Freed, 1973). The P line of rat was developed using bidirectional selection from a colony of Wistar rats at the Walter Reed Hospital (c.f., McBride and Li, 1998; Murphy et al., 2002). The general selection criteria for P versus alcohol-nonpreferring (NP) rats were that when given free-access to 10% ethanol and ad lib access to food and water, P progenitors would consume greater than 5 g of ethanol/kg of body weight/day and have an ethanol to water consumption ratio greater than 2:1, whereas NP progenitors would consume less than 1 g/kg/day and have an ethanol to water consumption ratio of less than 0.5:1 (c.f., McBride and Li, 1998; Murphy et al., 2002).

In a recent review on adolescent brain and behavior development, Spear (2000) indicated that the boundaries (i.e., beginning and end) of the adolescent "window" of neurobehavioral development for rats may differ given the parameters (e.g., behavioral, neurochemical, etc.) examined. However, neurobehavioral discontinuities between post-weanling and adult rats suggest that adolescence spans postnatal days (PND) 28 through 42 (i.e., 28 through 42 days old; Spear, 2000; Spear and Brake, 1983). This developmental window corresponds with timing of the growth spurt (Kennedy, 1967; Spear, 2000), changes in NMDA receptor binding of the prefrontal cortex (Insel et al., 1990), timing of emergence from the protected nest in the wild (Galef, 1981) and maturation of genitalia in female (Döhler and Wuttke, 1975) and male (Clermont and Perry, 1957) rats. Spear (2000) suggests that this conservative window (PND 28 through 42) could be extended through PND 60 when assessing the effects of pharmacological treatment during the "entire" adolescent period on adult behaviors in male and female rats. Our laboratory has published several studies using this window of ethanol treatment (PND 30 through 60). In one study, it was found that peri-adolescent P rats consumed more ethanol per kg body weight than their adult counterparts (Bell et al., 2003), with similar results found for peri-adolescent high alcohol-drinking (HAD-1 and HAD-2) rats (Bell et al., 2004). Another study using female P rats indicated that, compared with naïve P rats, P rats with access to ethanol during peri-adolescence (PND 30 through 60) displayed (a) quicker acquisition of operant self-administration of ethanol, (b) retarded extinction, and (c) greater operant responding during relapse, when tested during adulthood (Rodd-Henricks et al., 2002a).

As indicated above, our laboratory has reported that peri-adolescent P rats acquire adult levels (>5.0 g/kg/day) of ethanol [15% volume/volume (vol./vol.)] intake by PND 39 and that by PND 60 male P rats consume ~ 9.0 g/kg/day and female P rats consume ~ 7.5 g/kg/day (Bell et al., 2003). However, the pattern of ethanol intake displayed by peri-adolescent P rats or the BECs achieved at multiple time points across the day were not determined. When studied under 23 h access (1 h per day was devoted to laboratory procedures) operant conditions, it appeared that most of the ethanol self-administered by adult male P rats was not associated with feeding (Files et al., 1992, 1994), with only ~30% considered prandial-associated, and this percentage decreased substantially under limited access conditions (Files et al., 1994). As far as we know, only one study has examined free-choice, home-cage access ethanol drinking patterns in P rats, and this study was limited to adult male rats (Murphy et al., 1986). These authors (Murphy et al., 1986) reported that adult (>PND 90) male P rats ($n=4$) consumed approximately 70% of their ethanol during the dark cycle. Two of the 4 animals displayed a large bout at the end of the dark cycle (>1.0 g/kg/h), with all 4 animals displaying a bout at the beginning of the dark cycle and bouts in the middle of the dark cycle (Murphy et al., 1986). A bout is defined as a "cluster" of drinking/licking behavior that is sufficiently aggregated such that the organism must stop ongoing behavior in order to carry out this "cluster" of