Drug and Alcohol Dependence 119 (2011) 81–87

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Acute administration of vinpocetine, a phosphodiesterase type 1 inhibitor, ameliorates hyperactivity in a mice model of fetal alcohol spectrum disorder☆

Fernanda Nunes[a], Kélvia Ferreira-Rosa[a], Maurício dos S. Pereira[b], Regina C. Kubrusly[b], Alex C. Manhães[a], Yael Abreu-Villaça[a], Cláudio C. Filgueiras[a,*]

[a] Laboratório de Neurofisiologia, Departamento de Ciências Fisiológicas, Instituto de Biologia Roberto Alcantara Gomes, Centro Biomédico, Universidade do Estado do Rio de Janeiro, Av. Prof. Manoel de Abreu 444, 5 andar, Vila Isabel, Rio de Janeiro, RJ, 20550-170, Brazil
[b] Laboratório de Neurofarmacologia, Departamento de Fisiologia e Farmacologia, Universidade Federal Fluminense, R. Ernani de Melo 101, São Domingos, Niterói, RJ, Brazil

ARTICLE INFO

Article history:
Received 4 November 2010
Received in revised form 16 May 2011
Accepted 22 May 2011
Available online 9 September 2011

Keywords:
Ethanol
Alcohol abuse
Hyperactivity disorder
Alcoholism
Type 1 phosphodiesterase

ABSTRACT

Background: Maternal alcohol use during pregnancy causes a continuum of long-lasting disabilities in the offspring, commonly referred to as fetal alcohol spectrum disorder (FASD). Attention-deficit/hyperactivity disorder (ADHD) is possibly the most common behavioral problem in children with FASD and devising strategies that ameliorate this condition has great clinical relevance. Studies in rodent models of ADHD and FASD suggest that impairments in the cAMP signaling cascade contribute to the hyperactivity phenotype. In this work, we investigated whether the cAMP levels are affected in a long-lasting manner by ethanol exposure during the third trimester equivalent period of human gestation and whether the acute administration of the PDE1 inhibitor vinpocetine ameliorates the ethanol-induced hyperactivity.
Methods: From postnatal day (P) 2 to P8, Swiss mice either received ethanol (5 g/kg i.p.) or saline every other day. At P30, the animals either received vinpocetine (20 mg/kg or 10 mg/kg i.p.) or vehicle 4 h before being tested in the open field. After the test, frontal cerebral cortices and hippocampi were dissected and collected for assessment of cAMP levels.
Results: Early alcohol exposure significantly increased locomotor activity in the open field and reduced cAMP levels in the hippocampus. The acute treatment of ethanol-exposed animals with 20 mg/kg of vinpocetine restored both their locomotor activity and cAMP levels to control levels.
Conclusions: These data lend support to the idea that cAMP signaling system contribute to the hyperactivity induced by developmental alcohol exposure and provide evidence for the potential therapeutic use of vinpocetine in FASD.

1. Introduction

Maternal ethanol use during pregnancy causes a continuum of long-lasting disabilities in the offspring (Riley and McGee, 2005) commonly referred to as fetal alcohol spectrum disorder (FASD). It is estimated that the prevalence of FASD in school children may be as high as 2–5% in developed countries (May et al., 2009). Several neurobehavioral problems can be observed in FASD (Kelly et al., 2000; Kodituwakku, 2009; Riley and McGee, 2005), and attention-deficit/hyperactivity disorder (ADHD) is possibly the most commonly observed behavioral problem (Bhatara et al., 2006; Burd et al., 2003; Doig et al., 2008). It was estimated that as many as 41% of children with FASD have a comorbid ADHD diagnosis (Bhatara et al., 2006), while in studies considering children with fetal alcohol syndrome (FAS), which represents the most severe outcome of prenatal ethanol exposure (Goodlett et al., 2005; Riley and McGee, 2005), this percentage ranges from 73% (Burd et al., 2003) to 95% (Fryer et al., 2007).

Although the three main symptoms of ADHD, impulsiveness, inattentiveness and hyperactivity, have been modeled in rodents (Sagvolden et al., 2005), hyperactivity is the most frequently studied by far. Murine hyperactivity has been usually assessed in the open field test, which estimates ambulatory movements on a wide surface. Despite its simplicity, the measure of ambulation has proven to be a useful tool in studies designed to predict aspects of behavior, genetics, and neurobiology of ADHD (Lalonde and Strazielle, 2009; Sagvolden et al., 2005). Locomotor hyperactivity is a pivotal behavioral trait observed in several inbred strains, knockouts, and transgenic rodents used as models of ADHD (Russell, 2007; Sagvolden et al., 2005). In FASD rodent models,

☆ Supplementary Materials showing mortality rates and open field activity can be found by accessing the online version of this paper at http://dx.doi.org.

* Corresponding author. Tel.: +55 21 2868 8195; fax: +55 21 2868 8029.
E-mail addresses: ccfilg@pq.cnpq.br, ccfilg@yahoo.com.br (C.C. Filgueiras).

0376-8716
doi:10.1016/j.drugalcdep.2011.05.024