Pharmacology, Biochemistry and Behavior 143 (2016) 26–33

Contents lists available at ScienceDirect

Pharmacology, Biochemistry and Behavior

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

Chronic caffeine produces sexually dimorphic effects on amphetamine-induced behavior, anxiety and depressive-like behavior in adolescent rats

Sarah M. Turgeon [a,b,*], Shannon E. Townsend [b], Rushell S. Dixon [b], Emma T. Hickman [b], Sabrina M. Lee [b]

[a] Department of Psychology, Amherst College, Amherst, MA 01002, USA
[b] Neuroscience Program, Amherst College, Amherst, MA 01002, USA

ARTICLE INFO

Article history:
Received 2 September 2015
Received in revised form 29 January 2016
Accepted 31 January 2016
Available online 2 February 2016

Keywords:
Light/dark test
Elevated plus maze
c-Fos
Forced swim test
Open field test

ABSTRACT

Caffeine consumption has been increasing rapidly in adolescents; however, most research on the behavioral effects of caffeine has been conducted in adults. Two experiments were conducted in which adolescent male and female rats were treated with a moderate dose of caffeine (0.25 g/l) in their drinking water beginning on P26–28. In the first experiment, animals were maintained on caffeinated drinking water or normal tap water for 14 days and were then tested for behavioral and striatal c-Fos response to amphetamine (1.5 mg/kg). In the second experiment, rats were maintained on caffeinated drinking water or normal tap water beginning on P28 and were tested for novel object recognition, anxiety in the light/dark test (L/D) and elevated plus maze (EPM), and depressive like behavior in the forced swim test (FST) beginning on the 14th day of caffeine exposure. Caffeine decreased amphetamine-induced rearing in males, but had no effect in females; however, this behavioral effect was not accompanied by changes in striatal c-Fos, which was increased by amphetamine but not altered by caffeine. No effects of caffeine were observed on novel object recognition or elevated plus maze behavior. However, in the L/D test, there was a sex by caffeine interaction on time spent in the light driven by a caffeine-induced increase in light time in the males but not the females. On the pretest day of the FST, sex by caffeine interactions were observed for swimming and struggling; caffeine decreased struggling behavior and increased swimming behavior in males and caffeine-treated females demonstrated significantly more struggling and significantly less swimming than caffeine-treated males. A similar pattern was observed on the test day in which caffeine decreased immobility overall and increased swimming. These data reveal sex dependent effects of caffeine on behavior in adolescent rats.

© 2016 Elsevier Inc. All rights reserved.

1. Introduction

Caffeine is the most widely used psychostimulant with estimates of up to 80–90% of the adult population consuming caffeine daily, mostly in coffee, tea, and soft drinks (Heckman et al., 2010). At typically consumed doses, caffeine acts as an antagonist at adenosine receptors in the central nervous system (Fredholm et al., 1999). In adults, moderate doses of caffeine have been shown to have beneficial effects such as increased attention, mood, energy and cognitive performance (Smith, 2002; Einother and Giesbracht, 2013). However, the majority of studies on caffeine have been performed on adults and increases in marketing of caffeine products, such as energy drinks, to children and adolescents have lead to concern about the paucity of data addressing the effects of caffeine in adolescents (Temple et al., 2009; Ruxton, 2013; Owens et al., 2014).

A few studies have reported that caffeine produces different effects in adolescent and adult animals. Adolescence in rats has typically been defined as the period between P28 and P40 based upon the timing of the emergence of adult-like behavioral and neurochemical characteristics (Spear, 2000). Moderate acute doses of caffeine (10 and 30 mg/kg, ip) induced greater locomotor stimulation in adolescents (P37–40) than adults (Marin et al., 2011). Withdrawal from chronic caffeine (1 mg/kg in drinking water for 2 weeks beginning at P28 or P65–95) produced locomotor depression in adolescents but not adults and reduced the locomotor response to a challenge dose (30 mg/kg, ip) of caffeine (Rhoads et al., 2011), suggesting that the developing adolescent brain is more sensitive to long-term effects of caffeine exposure.

Caffeine has been shown to alter mood and anxiety in humans (Yamada et al., 2014) as well as animal models. Caffeine decreased immobility in the forced swim test (FST) in both control (El Yacoubi et al., 2003) and chronically stressed rats (Pechivanova et al., 2012), suggesting an antidepressant effect. Both acute and chronic caffeine exposure

Abbreviations: P, Postnatal day; L/D, Light/dark test; EPM, Elevated plus maze; FST, Forced swim test; FLI, Fos-like immunohistochemistry; ANOVA, Analysis of variance.

* Corresponding author at: Department of Psychology, Amherst College, Amherst, MA 01002, USA.
E-mail address: smturgeon@amherst.edu (S.M. Turgeon).

http://dx.doi.org/10.1016/j.pbb.2016.01.012
0091-3057/© 2016 Elsevier Inc. All rights reserved.

increased anxiety-like behavior in rats in the elevated plus maze (EPM; El Yacoubi et al., 2000); however chronic caffeine was found to decrease anxiety-like behavior in rats exposed to chronic unpredictable stress (Pechivanova et al., 2012). Caffeine exposure during adolescence has also been reported to increase emotional reactivity in adult rats (Anderson and Hughes, 2008). In a recent effort to address the paucity of data on the effects of caffeine in adolescents, Ardais et al. (2014) exposed adolescent male rats to caffeine in their drinking water beginning at postnatal day (PND) 28. Behavioral testing between PND 48 and 51 revealed decreased habituation to a novel environment, increased recognition memory as assessed by a novel object recognition test, and increased anxiety in the EPM. In addition, they reported alterations in cortical and hippocampal brain derived neurotrophic factor (BDNF) and adenosine A1 receptors (Ardais et al., 2014).

Data on sex differences in the effects of caffeine are limited; however, a study in humans reported that adolescent boys found caffeine more rewarding than girls (Temple et al., 2009). Another human study found an association between caffeine consumption and anxiety that was limited to males (Trapp et al., 2014). While we were unable to find evidence from animal studies for sex differences in the behavioral effects of caffeine, a number of the behaviors that are subject to alteration by caffeine in animals have been found to be sexually dimorphic. Sex differences in behavior have been noted in the EPM (Johnston and File, 1991; Lynn and Brown, 2009) and the FST (Dalla et al., 2009; Kokras et al., 2015). In addition, sex differences in the EPM and the light/dark test appear to be age-dependent (Turgeon et al., 2011). Caffeine also produces increased behavior in response to other psychostimulants (Cauli et al., 2003; Gasior et al., 2000; Simola et al., 2006a, 2006b). Females have been shown to have a greater behavioral response to amphetamine (Garrett and Griffiths, 1997; Hensleigh et al., 2011) and methylphenidate (Boeck et al., 2009) as well as greater striatal c-Fos induction following amphetamine (Castner and Becker, 1996; Snyder-Keller and Keller, 1998). In addition, amphetamine-induced behavior and striatal c-Fos are decreased by adenosine agonists (Turgeon et al., 1996), suggesting their potential for modulation by caffeine.

Given sexual dimorphisms in behaviors shown to be modified by caffeine, it seems reasonable to predict that sex differences in the effects of caffeine on these behaviors and amphetamine-induced striatal c-Fos might exist. Therefore, the present study examined the effects of exposing adolescent males and females to chronic caffeine on amphetamine-induced behavior and striatal c-Fos, object recognition memory, anxiety in the light/dark test and the elevated plus maze (EPM), and depressive-like behavior in the forced swim test (FST). Animals were exposed to caffeine in the drinking water to approximate the route of administration in humans and to prevent injection stress. The 0.25 mg/ml concentration of caffeine chosen was based on the observation by Gasior et al. (2000) that this concentration, but not a higher concentration, enhanced amphetamine-induced behavior in adult males. Amphetamine-induced c-Fos was assessed in both the medial and lateral striatum as the adenosine A2a receptor antagonist APEC decreased amphetamine-induced c-Fos in the medial striatum (Turgeon et al., 1996) whereas sex differences in amphetamine-induced c-Fos have been noted primarily in the lateral striatum (Castner and Becker, 1996).

2. Experimental procedures

2.1. Animals

Forty-eight male and 48 female Sprague–Dawley rats (Charles River) were run in two separate experiments. All rats were housed individually in hanging wire cages maintained on a reverse light–dark cycle with food and water available *ad libitum*. All procedures were approved by the Amherst College IACUC.

2.2. Experiment 1

2.2.1. Animals

Rats arrived at the facility on P24 and experiments began between P26 and P28 (Day 1). Beginning on Day 1, rats in the caffeine group had their water replaced with caffeinated water (0.25 g/l). Fluid consumption was measured every two days and animals were handled and weighed on Days 1, 7, 12 and 15 (test day; P40-42). Behavioral analyses were conducted between 9 am and 1 pm.

2.2.2. Open field

On Days 13 and 14, all animals were exposed to the open field (60 cm × 30 cm × 30 cm with a thin layer of bedding) for 10 min following an ip injection of 0.2 ml saline to minimize injection and novel environment stress. On Day 15 (P40-42), rats were injected with D-amphetamine (Sigma; 1.5 mg/kg in 1 ml/kg saline, ip) or saline (1 ml/kg, ip). Eight treatment groups were generated: male-water/saline (n = 6), male-water/amphetamine (n = 6), male-caffeine/saline (n = 6), male-caffeine/amphetamine (n = 6), female-water/saline (n = 6), female-water/amphetamine (n = 6), female-caffeine/saline (n = 6), and female-caffeine/amphetamine (n = 5; one animal was removed due to leg injury). Immediately following injection, rats were placed in the open field and activity was videotaped for 60 min.

Activity was scored by an experimenter blind to the treatment condition for the number of cage-crosses (rat moves from behind a marker 15 cm from one end of the open field across a marker 15 cm from the other end) and rears (rat raises both front paws above a marker 13 cm above the bottom of the cage).

2.2.3. Immunohistochemistry

One hour following behavioral testing (2 h following injection), animals were anesthetized with 1.5 mg/kg of a cocktail containing 72 mg/ml ketamine and 6 mg/ml xylazine (im) followed by 1.5 ml/kg of 100 mg/ml sodium pentobarbital (ip). Rats were perfused transcardially with 0.9% saline followed by 10% formalin. Brains were stored in formalin overnight and cryoprotected in 30% sucrose for approximately four days. Fifty micron sections were cut and stored in PBS at 4 °C until processing for c-Fos like immunohistochemistry (FLI). Tissue was preincubated in 2% goat serum in PBS for 30 min and incubated overnight in rabbit polyclonal anti-cFos antibody (Oncogene Science, Cambridge, MA) at a 1:10,000 dilution. Tissue was washed 3 × 10 min in PBS and incubated with biotinylated goat anti-rabbit secondary antibody (Vector) for 1 h. Tissue was washed 3 × 10 min in PBS and placed in avidin–biotin HRP for 1 h. Following 3 × 10 minute wash in PBS and one 10 minute wash in 50 mM TRIS, tissue was developed with a 3,3′-diaminobenzidine tetrahydrochloride substrate kit. The number of FLI-positive cells was counted in a 1.2 mm^2 area of the dorsomedial striatum (M) and the dorsolateral striatum (L; Fig. 1) at 10× in 3 striata per brain and averaged.

2.3. Experiment 2

2.3.1. Animals

Rats arrived at the facility on P24 and experiments began on P28 (Day 1). Beginning on Day 1, rats in the caffeine group had their water replaced with caffeinated water (0.25 g/l). Animals were weighed and fluid consumption was measured every two days. There were four groups created: male-water (n = 12), male-caffeine (n = 12), female-water (n = 12), female-caffeine (n = 12). Animals were run in 6 batches of 8 animals, two from each treatment group. For the object recognition test, the first batch was eliminated due to a change in the objects used, leaving 10 animals in each group. In the FST, a videotaping error resulted in the loss of one batch leaving 10 animals in each group for these analyses as well. All behavioral analyses were conducted

Download English Version:

https://daneshyari.com/en/article/2012615

Download Persian Version:

https://daneshyari.com/article/2012615

Daneshyari.com